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The Journal of Allergy

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The Journal of Allergy

VOL. I MAY, 1930 NO. 4

Original Articles

THE SAND FLY (CADDIS FLY) AS AN EXCITING CAUSE OF ALLERGIC CORYZA AND ASTHMA*†

II. ITS RELATIVE FREQUENCY

SALVATORE J. PARLATO, M.D.
BUFFALO, N. Y.

AT A RECENT meeting of the Society for the Study of Asthma and Allied Conditions, I reported the first case of allergic coryza and asthma due to the inhalation of the emanations of the sand fly.[1] These emanations consisted of minute hairs and scaly epithelia which were readily thrown into the air from the wings, body, and limbs of the fly during its brief span of adult life. They are so common and so numerous along the shores of Lake Erie and the Niagara River as to literally cover the ground. Many times as one motors along the lake shore, it is necessary to operate the windshield cleaner in order to maintain a clear vision as he drives through swarms of the flies. They are first seen early in June and disappear about the second or third week in September. It is interesting to note that the time of their appearance coincides with the pollinating seasons of the common grasses and ragweeds.

It occurred to me that more instances of sand fly hypersensitiveness would be found, particularly among those patients with a typical history of allergy in which a thorough clinical study and complete skin testing with the routine and well-known allergens failed to produce a clue as to etiology and among those patients with summer hay fever and asthma in whom treatment with pollen extracts rendered little or no relief. Consequently from April to December, 1929, I tested routinely all my cases of allergy with the extract of whole sand flies. The results of these tests in 192 cases will be offered at this time.

The extract of whole sand flies was prepared according to the method of Coca and Milford[2] and sterilized by passage through a Berkefeld filter. A clear dark brown solution of 1.12 mg. of nitrogen per c.c.

*From the Asthma and Hay Fever Department of the Buffalo Eye, Ear, Nose, and Throat Infirmary, Wettlaufer Clinic, Buffalo, N. Y.

†Read before the Academy of Medicine, Buffalo, N. Y., Dec. 11, 1929.

was produced. For testing, dilutions of 0.001, 0.01, and 0.1 mg. of nitrogen per c.c., respectively, were made up. Using the intradermal method, I injected 0.01 to 0.02 c.c. of the 0.001 dilution. If little or no reaction resulted, the 0.01 dilution was tried. The 0.1 dilution was seldom needed. A typically positive skin reaction was noted within five to fifteen minutes. No undue constitutional reactions happened at any time. The ophthalmic test was done by instilling a drop of the extract into the conjunctival sac. A positive reaction appeared within two to fifteen minutes and was characterized by a pronounced itching

Fig. 1.—Photomicrograph (×300). The emanations of the sand fly as shown here consist of the coarse type of hair, several portions of scaly epithelium, and a section of a wing. These emanations were collected by brushing the flies very gently over an 80-mesh sieve. They are so light and so readily carried by the air that a good part of these fine particles were lost in spite of due care in handling.

of the eye, lacrimation, and marked reddening of the conjunctiva. Controls were made in the skin and eyes of my office assistants, relatives, and friends of the patients. Whenever the skin and eye gave positive evidence of hypersensitiveness to the sand fly, confirmatory tests were made.

First was the clinical test. A very small amount of the desquamations and hairs of the flies, as shown in Fig. 1, was placed upon the conjunctival surface of either lower eyelid. A severe reaction, typical

of hay fever, quickly followed. Appropriate controls were also carried out by repeating this test at the same time on normal, nonallergic individuals. The second proof of specific sensitization is the passive transfer test. In the four cases in which the blood of the patient was available, the presence of the sand fly reagin was demonstrated in each serum.

The cases which were studied for this paper are made up of 164 private patients and 28 patients of the new Asthma and Hay Fever Department of the Wettlaufer Clinic and Buffalo Eye, Ear, Nose, and

Fig. 2.—Photomicrograph (×280). A portion of nasal secretion from a patient, placed on a glass slide a few minutes after handling the sand flies as related in legend under Fig. 1. Note the group of three hairs tenaciously held by the mucus. The characteristic salt crystals of the nasal secretions are readily recognized. This is another evidence of the viability of the sand fly emanations and that they are introduced into the body chiefly through inhalation.

Throat Infirmary. In every instance, skin tests with foods, pollens from trees, grasses, and weeds known to cause hay fever and asthma in Buffalo and suburbs, bacteria, animal emanations, feathers, etc., were made along with the skin and eye tests with the sand fly extract.

For the sake of easy analysis, I have divided these 192 cases of allergy into groups according to the principal complaint of each patient. The results of these tests, as indicated by Table I, show that 14, or 7 per cent, of the total tested cases gave positive skin and eye

reactions to the sand fly extract. Two patients who gave repeated skin reactions but negative eye reactions were not included. All those who were found hypersensitive gave a history of contact with great numbers of sand flies. As a rule, their homes were located near the Niagara River or Lake Erie either on the American or Canadian side.

TABLE I

DETERMINATION OF THE FREQUENCY OF SAND FLY AS AN EXCITANT OF ALLERGIC MANIFESTATIONS

1. Patients with summer hay fever symptoms only	
A. Number tested	65
B. Number of positive reactions*	5
2. Patients with bronchial asthma only	
A. Number tested	46
B. Number of positive reactions	3
3. Patients with hay fever and asthma	
A. Number tested	39
B. Number of positive reactions	5
4. Patients with hay fever, asthma, and some skin manifestation	
A. Number tested	10
B. Number of positive reactions	1
5. Patients with skin manifestations only	
A. Number tested	4
B. Number of positive reactions	0
Total cases tested 192	Total positive sand fly cases 14

*As denoted by typical positive reactions of skin and eye to sand fly extract of 0.001 to 0.1 milligram of nitrogen per c.c.

TABLE II

SINGLE OR MULTIPLE SENSITIZATION

TOTAL NUMBER OF POSITIVE SAND FLY CASES	14
A. Number reacting to sand fly only	6
B. Number reacting to sand fly and other air-borne allergens	6
C. Number reacting to sand fly and foods	0
D. Number reacting to sand fly and bacteria (respiratory type)	2

The 14 positive cases were divided into two classes, according to whether they demonstrated single or multiple sensitization. A significant fact which may be noted from Table II is that 6 patients reacted only to sand flies and 2 to sand flies and bacteria (respiratory types), making a total of 8 cases in which the primary exciting agent was the emanations of the Caddis fly. Its importance as an etiologic factor in asthma and hay fever is quite apparent. The 6 other positive reactions were obtained in patients who also reacted to other air-borne substances, such as pollens, animal danders, orris root, silk, etc. In this latter group, failure to treat with sand fly extract would materially reduce the chances for success in treatment. This may undoubtedly explain why some of our summer hay fever and asthma cases with positive evidence of pollen hypersensitiveness do not get

along satisfactorily with just the injections of pollen extracts. This is illustrated in the accompanying case reports:

A man, twenty-one years old first consulted me in July, 1928, for treatment of hay fever which started in June and ended in September. He gave positive skin reactions to the pollens of grasses and ragweeds. The usual pollen injections were given but only partial relief resulted. In April of the next year (1929) when he reported for his preseasonal pollen injections, he was tested with sand fly extract. The skin and eye gave distinctly positive reactions, even stronger than those which the pollens had produced. Subsequently, sand fly extract was given along with the pollen injections and complete relief from his hay fever resulted.

A girl, eight years old, came in the latter part of October, 1928, for treatment of bronchial asthma which started when she was three years old. Attacks occurred throughout the year but were worse during the summer months. She reacted markedly to cat hair, horse hair, and duck feathers and only slightly to the two ragweeds. I thought that the latter accounted for the fact that her condition was

Fig. 3.

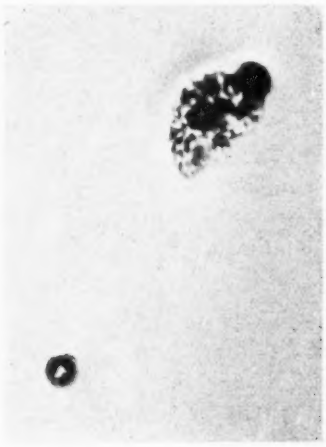

Fig. 4.

Figs. 3 and 4.—These two photomicrographs (×390) were made from two separate microscopic fields but from the same glass slide. The hair and scaly epithelium of the sand fly which are shown here, were identified in a sample of dust from the inside surface of a window screen in a home about one and one-half miles from Lake Erie. The sand flies in their efforts to get indoors strike against the window screens so that the emanations can easily get inside the home.

worse during the summer. She was inoculated with the extracts to which she reacted and went along without any asthma until July 14, 1929, when she was seized with severe paroxysms of dyspnea. She was spending her vacation on the Canadian lake shore and had asthma every night that she was there. Skin and eye tests showed that she was markedly sensitive to sand flies. Moving away from the lake shore gave her immediate and lasting relief. Next spring she will be given injections of sand fly extract as a prophylactic measure.

In Table III, the cases with positive sand fly reactions are divided according to the time of the year when symptoms of allergy occurred. Attention is called to the fact that 9 reported that their asthma or hay fever occurred only during the summer months. While the other 5 had paroxysms through the year, they were decidedly worse during

the summer when the caddis fly is found in such great numbers. During the rest of the year, the flies are found in the sweepings from attics, garages, vacant rooms, etc.

TABLE III

THE SIGNIFICANCE OF THE SUMMER MONTHS IN THE POSITIVE SAND FLY CASES*

NUMBER OF POSITIVE SAND FLY CASES	14
1. Cases with symptoms of allergy during the summer months only	9
2. Cases with symptoms of allergy throughout the year	5
A. Made worse during the summer months	5
B. Symptoms unchanged during the summer months	0

*It is to be remembered that the sand fly is seen from about the first or second week in June until about the third week in September.

DISCUSSION

It is believed that a large portion of the population of the United States and Canada reside near the Great Lakes and the many rivers which either lead into or out of these lakes. Because the natural habitat of the sand fly is near the shores of these lakes and rivers,[3] millions of people are annually exposed to myriads of these flies. From summer to summer, the people have recognized them as inevitable pests. Our present studies indicate that these flies are not a rare cause of asthma and hay fever but are sufficiently common to constitute a menace to public health. While 14 positive cases may seem a great deal, one must remember that most of my patients came in during the summer months and that my practice is mainly made up of asthmatics who live near Lake Erie, Lake Ontario, or the Niagara River. Figley[4] in a recent article reported 4 cases of asthma due to the pellicle shed by the May fly which is found in swarms in and about Toledo, Ohio. It is possible that hypersensitiveness to other common flies may be demonstrated in the near future.

SUMMARY

1. Routine skin and eye tests with the whole sand fly extract in 192 cases of allergy have revealed 14 patients with positive reactions. The 4 positive cases in which the passive transfer test was done, elicited the presence of sand fly reagin in their blood sera.

2. The comparative frequency of sand fly hypersensitiveness warrants its use as a routine test in all patients with allergic conditions, particularly those patients living near lakes, rivers, and ponds. In this way, I feel that many of our patients, especially those with summer hay fever and asthma, will more often be successfully diagnosed and treated.

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REVIEW OF THE HAY FEVER LITERATURE OF 1929*

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THE increasing interest in hay fever in America and foreign countries has resulted in a rather extensive literature on the subject. The existence of a large number of articles in foreign languages makes a periodic review almost a necessity. In this review, as in the previous one, I have tried to be as complete as possible, although several articles were omitted because they were not available. Again I wish to emphasize that the nature of the material of some articles, such as tabulations, illustrations, and similar conditions, do not lend themselves for abstract purposes, and in such instances the reader is urged to consult the original. In this connection, I may also say that in this review the space allotted to each individual paper is not in proportion to the worth of the latter.

Duke[1] has again reviewed the recent literature on allergy in an interesting, critical and authoritative manner. It is an important and informative piece of work for anyone interested in allergy. For a summary of the hay fever literature for 1927 and 1928 it would be advisable to refer to my previous review.[2] As in the past there are a number of articles[3, 4] which are summaries or repetitions and which add nothing new. However, the majority of the contributions add something to our interest and knowledge.

ETIOLOGY

Thiberge[5] concludes the report which he and Scheppegrell have previously presented on the prevalence of hay fever in South America. This report is based on the result of a letter of inquiry to various officials of these countries. Brazil replies that no case of hay fever has come to the attention of the physicians consulted. From Chile the report states that there are no cases among the natives, but foreigners who have contracted it before coming there will suffer as much as in any country. From Ecuador we have the information that there is no definite hay fever there, but that they have "epidemic catarrh" in February, March, April and May. These reports are contrary to what we might expect from our present knowledge of hay fever, and it is my opinion that our judgment as to hay fever conditions in South America should be delayed until more exact information can be obtained.

Balyeat[6] believes that pollen may cause perennial hay fever by pollen saturated articles in the home. On the other hand he emphasizes

*From the Asthma and Hay Fever Clinic, Northwestern University Medical School.

the fact[7] that many seasonal pollen cases are also sensitive to other substances, such as epidermals, or foods. These secondary factors tend to make the hay fever worse. In a series of 719 cases of hay fever he found pollen as the sole reactor in only 52.1 per cent. In 35.3 per cent there were marked reactions to animal dander, 10.4 per cent reacted to oris root, and 6.1 per cent were sensitive to foods. Although there might be objection to this high percentage of positive reactions because of the use of the intradermal method, it is now quite generally agreed that such complicating sensitizations are quite frequent and important to discover.

Foskett[20] also mentions the importance of checking up for reactions to other irritants than pollens alone in cases in which the ordinary pollen therapy is unsatisfactory. Garrett[39] also thinks that food sensitization is an important complicating factor in seasonal asthma.

It has been noted by Balyeat,[6] Gutmann[41] and others that the general health of the hay fever patients or other allergics is better than that of any other group of individuals.

There are several reports on the association of other lesions with hay fever or hyperesthetic rhinitis. Adlersberg and Forschner[8] found 14 pathologic gastrointestinal tracts in a series of 17 cases of hyperesthetic rhinitis; in eight of these the nasal condition was improved after treatment of the intestinal tract. In another series of 9 cases of chronic intestinal infections there were 2 cases of definite and 3 of apparent rhinitis. The typical findings in the intestines in the vasomotor rhinitis group were those of chronic constipation and its secondary effects. They also cite a case of hay fever which was benefited by gastrointestinal management.

Kaupe[9] reiterates the old observation of the relation of hay fever to "exudative diathesis" (eczema and asthma). Druesne and Verain[10] describe the case of a French woman who had her first attack of pollen asthma in 1922; and afterward, every season beginning about May 20, she had additional symptoms of urticarial plaques in the mouth and pharynx. The blood reaction was P_H 7.08. She was given alkalies, changing the reaction to P_H 7.49 with marked improvement within a few hours.

Gibb[11] describes the case of a seven-year-old girl who was stung by a bee and who immediately had an attack of generalized urticaria, hay fever symptoms, and asthma. The author maintains that this allergic shock was due to the transmission of the pollen by the bee sting, since no natural exposure to pollen was likely because all the wind-pollinated plants in the district were past the pollination stage. It seems to me that the above explanation is rather dubious, since insect-sting anaphylaxis has been reported a number of times, the child apparently never had hay fever symptoms previously or subsequently, and this reaction occurred outside of the pollen season.

Hays[12] says that there is a definite nervous system complex in all cases of hay fever, and that the nervous stability is greatly influenced by gastrointestinal and nasal pathology. Carmody and Greene[13] maintain that without infection in the sinuses or without pathologic membranes, the pollen dust and similar irritants do not produce hay fever. Similar views are held by McDonagh,[14] who has an additional theory of colloidal alteration of the blood.

A rapid and convenient method for skin testing with pollens is described by Henry;[62] dropper bottles are used, and tests on the skin are made in the same order as the arrangement of bottles and arrangement of pollen names on mimeographed sheets.

That seasonal hay fever may be due to substances other than pollen must be taken into consideration. Balyeat[6] mentions a case of periodic hay fever occurring every spring which was due to contact with dog hair during the spring cleaning of dog kennels. In a short article[16] I have described two cases of seasonal hay fever occurring over a number of years and due entirely to orris root.

BOTANICAL STUDIES

Durham[17] made a comparative study of the ragweed pollen in 22 cities with collaboration of a number of allergists. He concludes that ragweed pollen is more abundant in agricultural districts and least in large cities and those removed from agricultural districts. The ragweed season is earlier in the northern part of the United States than in the South. Storm periods and consequent high winds are responsible for periods of heavy pollen incidence. The dates of onset and close of the pollen season in any particular district do not vary appreciably from year to year.

In New England, Fishbein[18] says hay fever is divided into three seasons: March to May, due chiefly to cottonwood, black walnut and oak; middle of May to middle of July, due to June grass, orchard grass, timothy, and red top grass; and early August to middle of September, due to ragweeds.

In a preliminary report of a pollen survey of Indiana, Durham[19] divides the hay fever season into three parts. The early spring season due to trees is caused by oak, box elder, walnut, birch, sycamore, cottonwood, maple, hickory, and pine (in the order of their importance). The midsummer season is caused chiefly by June grass, orchard grass, red top grass and timothy. In the late summer season the short and giant ragweeds are of greatest importance. In the southeast portion of the state southern ragweed is found, and in the extreme northwest portion burweed marsh elder. In the river bottom land of the southeast part of the state marsh elder is found. In a report of the hay fever conditions in Willamette Valley, Oregon, Foskett[20] thinks the following wind-pollinated trees of importance: birch, alder, maple, box

elder, willow, hazelnut, cottonwood, beech, and ash family. The midsummer hay fever plants are the grasses. He says the weeds of importance are: dock weed, lamb's quarters, plantain, pigweed, sheep sorrel, thistle, and others.

Rowe[21] has made a thorough botanical survey of San Francisco and its vicinity. Because of the tables and detailed data it is practically impossible to abstract this paper. In general, it may be said that the most common plants are grasses, chenopodiaceae, artemisiae, and trees (especially oak, birch, sycamore and acacia).

An interesting addition to our list of hay fever producing pollens is made by Sellers,[22] who reports several cases sensitive to the mesquite tree pollen. This tree is native to Texas and begins to bloom about the middle of April, and most trees are in full bloom the first week in May. They continue to bloom until late in July. He claims good results with treatment with this pollen.

Cedar hay fever, according to Black[23] is found to be a common condition throughout the central and eastern parts of Texas and extends to some extent toward the southwest. It is caused by the pollen of the mountain cedar, Juniperus sabinoides. Pollination begins from December 20 to January 1 and continues into or through February.

In the vicinity of Melbourne, Australia, Derrick[24] finds the following plants the most important causes of hay fever: rye grass *(Lolium perenne)* and cocksfoot grass *(Dactylis glomerata)*, pollinating from September to January inclusive; prairie grass *(Bromus unioloides)*, pollinating from September to November; and capeweed *(Cryptostemma calendulacea)*, from August to November.

POLLEN CHEMISTRY AND OTHER POLLEN STUDIES

Arguing that various methods of extraction and purifying pollen may denaturize the latter, Murphy[25] has employed pollen suspensions prepared as follows: The pollen is macerated, the mass is sterilized with phenol, and suspended in buffered salt solution containing 0.5 per cent phenol as preservative. The injections with these suspensions are well tolerated, are no more painful than clear extracts, and are rapidly and completely absorbed. The reactions are typical but apparently not stronger. Ten cases were treated with approximately the same results as with clear extracts.

Grünewald,[26] calling attention to the fact that the natural method of extracting the pollen is by the flower which it fertilizes, proposes a method of extraction in which the flowers with the contained pollen are extracted. He treated himself with such extract by the intradermal method with perfect results.

The resistance of pollen to extremely low temperatures was demonstrated by Becquerel[27] when he exposed the pollen of *Antirrhinum majus* and *Nicotiana tabaccum* for seven hours in liquid helium at a

temperature of – 271° C. Later the pollen was put in glucose at 25° C., and it was found that from one-third to one-half of the pollen was viable, showing germination.

Chemical studies on pollen were made by Loeb.[28] He found that it was possible to sensitize guinea pigs against watery extracts and alcohol precipitates of pollen of *Pinus silvestris*. The aqueous extracts contained considerable nitrogen, one-half of which was precipitated with FeOH (colloid dispersive) and one-half molecular dispersive; the extracts also contained reducing substances. The alcohol precipitate contained only colloid dispersive nitrogen and only traces of reducing substances. Sensitization with alcohol filtrate was impossible. Pursuing his chemical studies with the pollen of foxtail grass *(Alopecurus)* he found[29] that the alcohol precipitate gave positive reactions on the skin of hay fever patients while the alcohol filtrate gave no reaction. A solution of the alcohol precipitate and the total extract subjected to tryptic digestion gave no positive cutaneous tests. He concludes that the active principle of pollen extract is protein or closely bound to a protein or only effective when bound to a protein.

Several studies have been presented dealing with the identity of pollen atopens. Chobot[30] demonstrated in 10 timothy cases an equal sensitiveness to Bermuda grass by dilution methods. Local sensitization of the normal skin by passive transfer and desensitization with timothy pollen extract also desensitized to Bermuda pollen. He thinks the atopens are identical and advises patients who go South for the winter to keep up with timothy extract desensitization. Black[23] reports the treatment of 40 cedar hay fever cases. He obtained excellent results both with mountain cedar pollen and the pollen of Port Orford cedar, the latter of which does not grow in Texas but is native to Oregon and California. He concludes that there is a group antigen for the cedar pollen.

As opposed to the above, Benjamins et al[31] claim to have demonstrated that the atopens of various grass pollens are not identical. They have hyposensitized the skin of hay fever patients with pollen extracts of one species and then tested the same skin area with extracts of other species of pollen and obtained strong reactions.

Rappaport and Johnson[32] report experiments on fractionation of pollen proteins and their skin reactions on skin sensitive individuals. In the group sensitive only to the common ragweed protein the reaction was practically to the globulins alone. In the group sensitive to both ragweeds, skin sensitivity to the common ragweed still showed a preponderance of reaction to the globulins while reaction to the giant ragweed was almost completely limited to the albumin fraction. The evident criticism to this work is that these authors claim that of 40 ragweed patients 20 were sensitive to common ragweed only and 20 were sensitive to both giant and common ragweeds. This finding is,

of course, entirely contrary to the accepted and reported findings of all allergists who can demonstrate a sensitiveness to both ragweeds in a majority of cases.

Wodehouse[33, 34, 35, 36] has made a number of important contributions in the study of pollen characters as a means of classification of plants. He says that pollen-grain characteristics are useful in determining phylogenetic relationship. He maintains that the characters of pollen grains may be divided into two classes—the emphytic characters which are usually strictly phylogenetic and consequently of high diagnostic value, and the haptophytic cell characters which are of much less diagnostic value but are of histogenetic interest. Numerous beautiful drawings and classifications make these reports of inestimable value and interest, and the reader is urged to consult the original.

SPECIFIC TREATMENT

Numerous reports are present[40, 41, 42] emphasizing the continued and increasing success with specific desensitization therapy. Wilmer[37] favors the long interval method of treatment; Manning speaks of individualization of dosage as a requisite for high percentage of good results.

Gatterdam[43] says that intradermal seasonal treatment is of decided benefit and many times can replace preseasonal treatment, and the intradermal method may also be used preseasonally. Van Leeuwen[44] recommends in some cases frequent injections, even twice daily. He says further[45] that it is sufficient to use only two mixtures of extracts, a grain mixture and a weed mixture (in Holland); that one can expect only reduction in sensitivity and not complete desensitization. He uses tuberculin treatment along with pollen extracts.

Murphy's[25] report on the use of pollen suspensions in treatment of hay fever has already been mentioned. Balyeat[7] emphasizes the importance of avoidance of, or treatment with, the secondary factors in seasonal hay fever, such as orris root, animal dander and foods. He says also that he believes that many seasonal hay fever cases require desensitization against one or more groups of pollens other than the one whose season of bloom corresponds to the period over which the patient suffers.

Group Antigens.—There is increasing evidence that group antigens are present in pollens and that one species may be used in treatment for exposure of another species. Thus, Chobot[30] recommends the use of timothy extract for treatment against Bermuda grass. Black[23] obtained excellent results by treating mountain cedar hay fever cases with pollen of Port Orford cedar to which the patients have never been exposed.

On the other hand, Henderson[46] writes that grass sensitive cases who failed on timothy treatment became successful on mixed grass pollen

treatment. Benjamins[47] says that it is not sufficient to treat grass pollen cases with one or two of the species of grass pollens. He proves his contention by skin tests. He uses (for the region of Utrecht) a mixture of the seven most effective grass pollens; two parts *Festuca rubra* and one part each of *Arrhenatherum elatius, Holcus lanatus, Secale cereale, Alopecurus proteus,* and *Lolium perenne.* Petow and Loeb[49] (Germany) compared grass pollen mixtures with timothy pollen extract alone in treatment and found better results with the mixed pollens.

Complications of Treatment.—Kahn[50] cites the case of a multipara, aged thirty years, who had a marked systemic reaction following the injection of 0.7 c.c. of 1:20 timothy extract. This reaction, in addition to the common symptoms of urticaria, hay fever and asthma, consisted of excruciating pains in the lower abdomen which she described as identical with labor pains. The patient was about one week pregnant but did not miscarry.

Three cases of fatal anaphylaxis are described by Lamson[61] from the reports of other physicians. One of these was a pollen sensitive patient with perennial hay fever who occasionally had mild attacks of bronchial asthma. He was treated with Bermuda grass pollen and obtained marked relief from his hay fever. He received the fifteenth injection consisting of 0.05 c.c. of 1:100 on the twenty-fourth day of treatment. An asthmatic attack occurred and death resulted in three to five minutes.

Eisner,[48] in going to the country during pollination time in the spring, noticed a sudden onset of pain in his left arm which he had injected for three seasons with pollen extracts. In addition to that there was itching at that site, and pressure there produced hematomata. Two years later he began treatment with timothy and rye pollen extracts and noticed a recurrence of the neuritis with the first injection.

Atypical Types of Hay Fever.—An extremely interesting and instructive paper by Wilmer[15] classifies some of the atypical cases found in reviewing a series of 1900 cases of hay fever. One class consisted of 44 cases having definite hay fever symptoms with no positive skin or conjunctival tests: 32 of these were relieved by pollen therapy. In 30 cases of seasonal asthma without hay fever symptoms and with positive skin tests, 25 were relieved. In 10 similar cases with negative skin tests only 5 were relieved by pollen treatment. In 2 cases of hay fever with seasonal bladder tenesmus and urinary frequency the symptoms were relieved by removal of all uncooked vegetables. In 4 cases of generalized eczema with negative tests to all proteins except pollens and with no hay fever symptoms, 3 obtained relief by pollen desensitization with no relation to seasons. In 4 cases of marked dermatitis with positive skin tests to the pollens and no hay fever symptoms, all of them were improved by pollen therapy.

Twenty-five hay fever patients who failed to be relieved by the preseasonal, long interval method were treated the following year by receiving daily injections for two weeks, and then an injection once weekly for the entire season. Of this number 19 were relieved.

Wilmer also mentions cases of perennial rhinitis with positive skin tests to pollens only in whom he was able to prove that their paroxysms were due to contact with pollen which had been harbored in books, floor coverings and similar protected places.

Of 40 cases having asthma, hay fever and positive skin tests who had not been relieved by pollen treatment alone, 25 were relieved by the addition of an autogenous vaccine to the regular treatment.

Rackemann[51] has analyzed a series of hay fever patients with respect to "cure," or freedom from symptoms for two seasons without treatment. Out of 410 ragweed patients treated prior to 1925, twenty-six could be placed in that class. About one-half of the total cures have occurred among those patients who were treated for only one year. He concludes that patients who must have treatment for more than five years are rarely cured. The cure does not depend upon the total number of years of treatment nor upon a particular technic of treatment. In one-half of the patients with cures the skin tests were still positive. In grass cases there were about 7 per cent cures.

NONSPECIFIC TREATMENT

Beckmann[52] continues to report on the use of nitrohydrochloric acid in the treatment of hay fever. A total number of 185 cases were treated by 26 physicians (including Beckmann) during 1928. Of this number 75 obtained complete relief, 47 marked relief and 63 no relief. He remarks that these results compare favorably with desensitization treatment. However, it may be significant to note that the physician treating the largest number of cases, thirty-three, obtained relief of any degree in only six of them. Beckmann thinks that hay fever is a state of alkalosis and makes a number of assertions contradicting many known and established facts in allergy. He proposes the dramatic suggestion "that a clean start be made in the study of allergy, the new researches to be based upon the assumption that the allergic individual is one who at all times is in a state of relative alkalosis."

Duke[1] says that he has rarely obtained pronounced benefit in hay fever from the internal administration of nitrohydrochloric acid. My experiences over a period of two hay fever seasons coincide very closely with those of Duke.

Gatterdam[43] suggests the use of luminal or bromides to counteract the nervousness caused by ephedrin. A further favorable report is presented on the use of salvamin by Poras of Vienna.[53] My limited experience with this drug in the past season has been very disappoint-

ing. Sternberg[54] maintains that some types of hyperesthetic rhinitis or hay fever are made worse by adrenalin or cocaine locally.

Diathermy with special nasal electrodes is recommended by Hamm[55] and ultraviolet locally by means of special home made apparatus are advocated by Nagel[56] and Salmony.[57] None of these reports present data or results, and are very unconvincing.

Most allergists agree that nasal surgery should rarely be done in allergic patients. Guyton[58] says that operations on the nose should be done chiefly for gross septum deformity and sinus infection. There is a great tendency for operated patients to get worse.

Carmody and Greene[13] recommend local treatment of hay fever. In their series 77 responded to the simple ichthyol tampon, 19 to simple puncture of one or the other or both maxillary sinuses, and 5 to the radical operation on the maxillary sinuses and exoneration of the ethmoids. Emerson[59] favors local treatment.

Weiss[60] is even more radical in his views. He thinks that practically every case of hay fever has underlying nasal pathology, and he advises turbinectomy, removal of polyps and removal of redundant mucous membrane. He does, however, apparently believe in pollen therapy because the closing sentence of his paper is "inoculations against hay fever should be preceded by removal of nasal obstruction."

McDonagh[14] claims miraculous results by the use of nonprotein diet, high colonic flushings, physics, and vaccines made from intestinal bacteria. Hays[12] believes that hay fever may be explained on the basis of a nervous disturbance due to intestinal dysfunction and nasal pathology and therefore advises the building up of the patient's constitution, the administration of 5 grains of salol three times daily and a remedy of the nasal factors. He also adds, however, that "three months before the season the patient should be tested with pollen and treatment with pollen extracts begun."

SUMMARY

The most significant advances in the 1929 literature on hay fever may be enumerated as follows:

1. The further increase in percentage of good results in treatment by more general recognition that other sensitizations, such as foods, epidermals, etc., may be complicating, or even the only, factors in seasonal hay fever.

2. The admission by some of the most enthusiastic advocates of local therapy or nasal surgery that pollen injections have their place in treatment of hay fever.

3. The continued increase in reports of hay fever surveys from various sections of the world, and the addition to our list of hay fever producing pollen.

4. More thorough analysis of series of cases, especially from the standpoint of "cures."

5. Further chemical studies.

6. Extensive studies on atypical cases of hay fever, such as hay fever without positive diagnostic tests, and perennial rhinitis due to pollen harbored in protected places in the home.

7. The increasing and more widespread realization of the fact that pollen desensitization, although not a perfect treatment, is the most effective means at our disposal for the treatment of hay fever.

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SUDDEN ALLERGIC REACTIONS IN THE MAXILLARY SINUS

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THE fortunate coincidence of a sudden asthmatic attack occurring during a progressive study of the sinuses with x-ray and opaque media, resulted in the observation that an apparently normal sinus membrane may increase in thickness to a centimeter or more within a few hours' time.

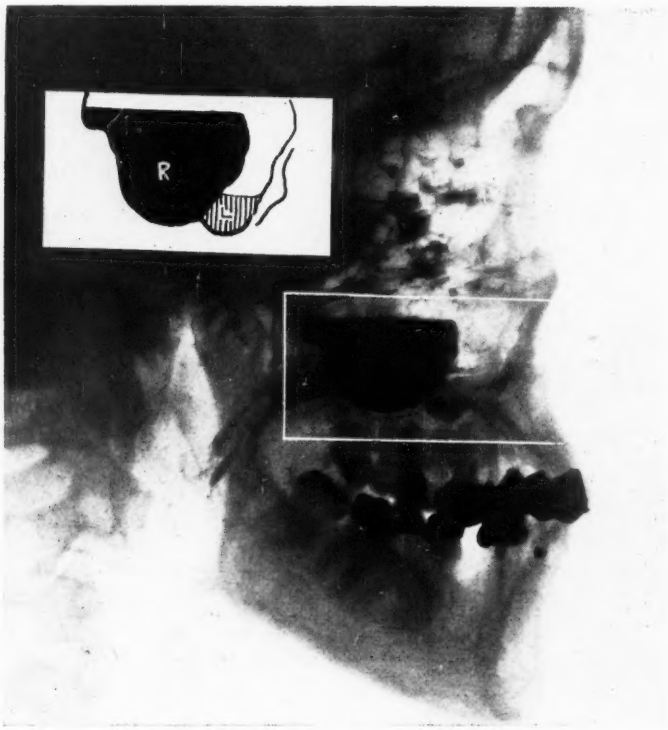

Fig. 1.—Case I. Lateral film made immediately after filling by displacement. The large amount of fluid in the right antrum had been introduced through a trocar a few days before. Note apposition of oil to cell wall throughout.

A patient suffering from occasional severe attacks of respiratory embarrassment was referred for nasal examination. From the history a diagnosis of asthma had been made, but no positive skin reaction could be obtained. The nasal examination was negative except for a slight general pallor of the mucosa and the presence of a few eosinophiles in the scant secretions. Before I saw the patient, routine

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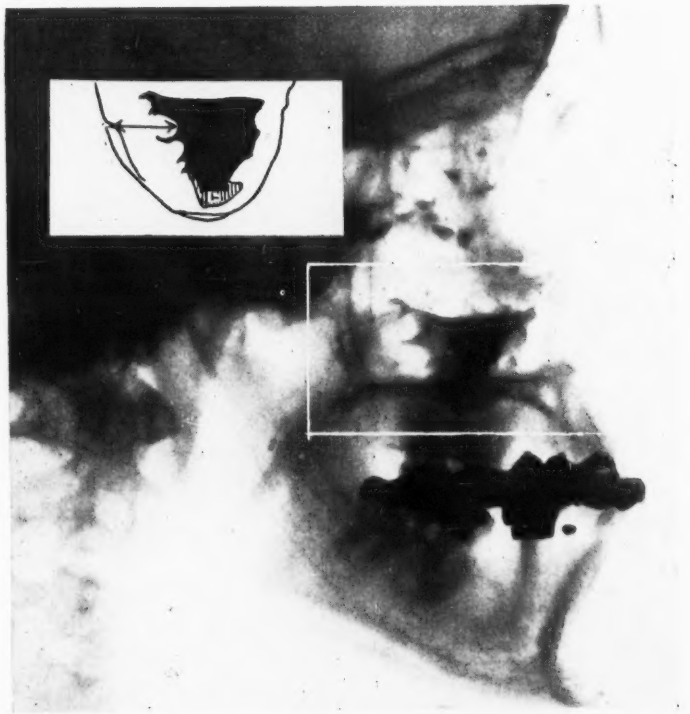

Fig. 2.—Case I. Lateral film made seventy-two hours after Fig. 1 and twelve hours after acute asthmatic attack. Note the extreme thickening of the mucosa indicated by the arrow in the diagram.

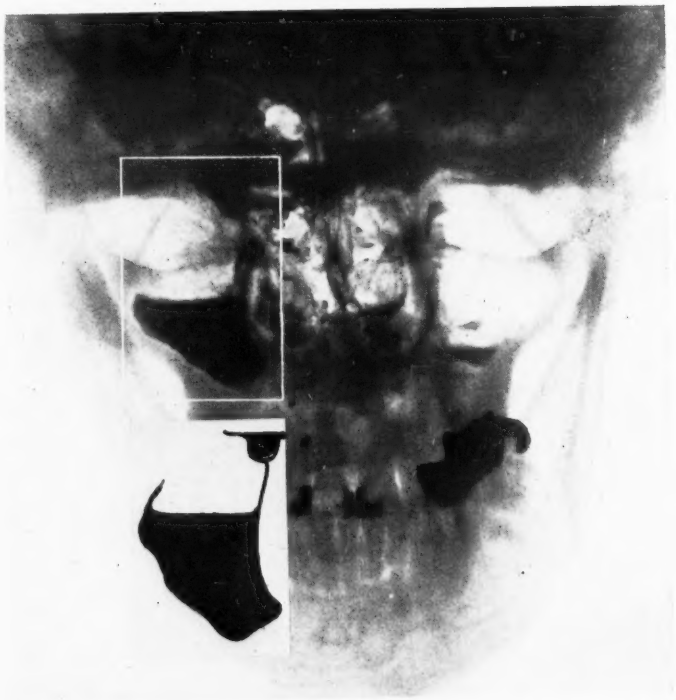

Fig. 3.—Case I. Posteroanterior view of Fig. 1. Note again the thin membrane in the antrum and also in sphenoid and ethmoid cells above.

x-ray films had been made which were negative. A mixture of equal parts of lipiodol and olive oil had been introduced into the right antrum through a trocar, puncturing the wall of the inferior meatus. The radiopaque mixture was in apposition to the sinus wall throughout, that is to say, the membrane was thin and there were no filling defects. It is our practice to fill the sinuses by the displacement method (gravity and intermittent vacuum), to make an immediate series of films and a second series seventy-two hours later, to determine the relative drainage of the cells. In this case, the first series showed no abnormalities (Figs. 1 and 3). The right antrum still retained most

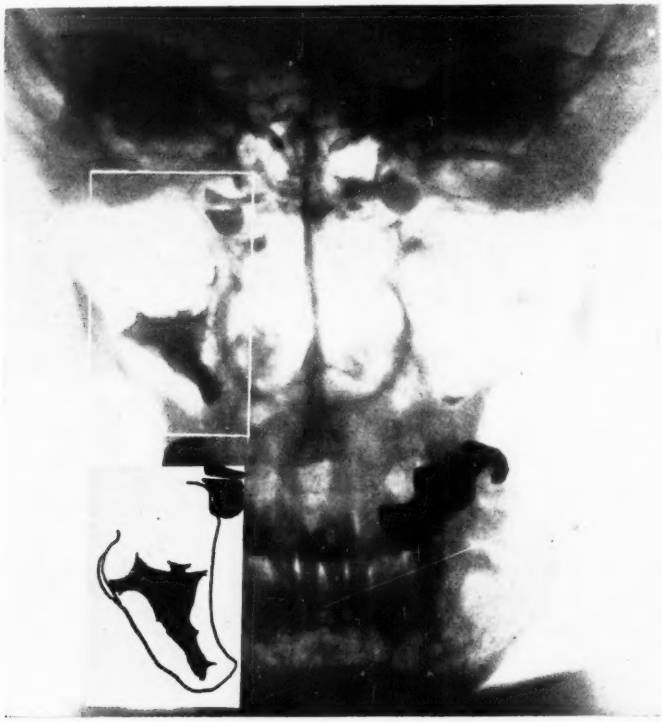

Fig. 4.—Case I. Posteroanterior view of Fig. 2. Note extreme thickening of antral mucosa while that of ethmoid and sphenoid remains unchanged.

of the injected oil. The patient was permitted to leave the hospital pending the second series.

On the night preceding the second examination, she slept on a goose-feather pillow; she had a severe asthmatic attack without any nasal disturbance; and on the following morning x-rays showed the antrum half obliterated by the mucosa which was swollen to the thickness of more than one centimeter. Most of the oil had been extruded; that which remained indicated a much restricted cavity and bore the concave outlines characteristic of polypoid degeneration of the mucosa (Figs. 2 and 4).

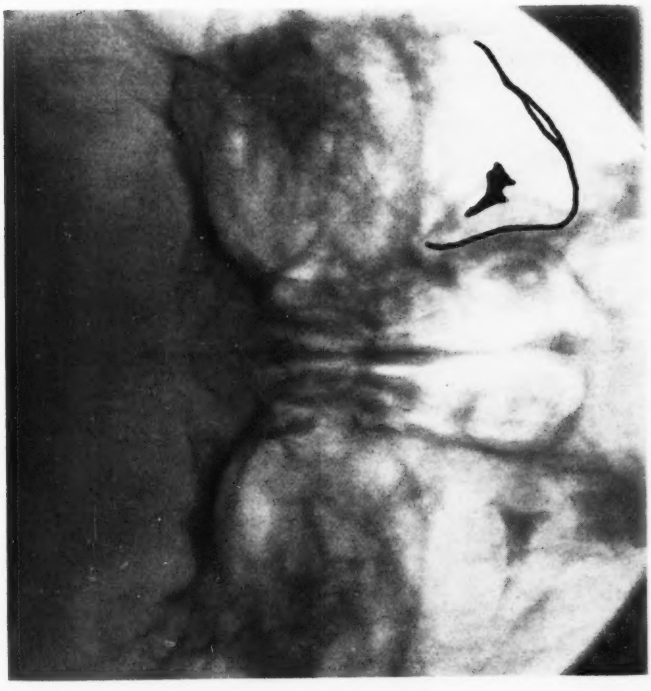

Fig. 6.—Case II. Seventy-two-hour film of the preceding.

Fig. 5.—Case II. Initial film. Right antrum is unretouched. The left is diagrammatically represented.

That the swelling was not due merely to an irritation by the opaque medium or to any idiosyncrasy to poppy-seed oil or olive oil is indicated by the fact that this had been in the antrum for several days preceding the attack without causing any thickening, and that the change came coincidentally with the asthmatic attack.

Examination of the film showed that the reaction was confined, so far as the nose is concerned, to the right antrum. The ethmoids, the sphenoids, and the opposite antrum were not affected, nor were there any symptoms of nasal obstruction during the attack or afterward. Why the swelling should remain thus localized I cannot say. It has

Fig. 7.—Case II. Lateral view of Fig. 5.

been suggested that the trauma of injecting the first dose of lipiodol, which was not present in the other sinuses, may have been a factor.

The following notes were made by Dr. C. H. Eyermann during his observation of the case:

"Mrs. C. M. F., seen September 28, 1929. History of winter colds since 1918, which consist of mild nasal blocking, nasal discharge, usually colorless, and sneezing. No itching. Summers: Always been well until this summer when nasal symptoms persisted throughout the summer. Patient is allergic individual, in that the ingestion of quinine is followed by urticaria. Mother and two maternal cousins also have idiosyncrasy to quinine, as has the patient's oldest child. Four paternal uncles have bronchial asthma. She has always had asthma, in addi-

tion to her nasal symptoms, at or immediately following Thanksgiving, Christmas and New Year's and during the month of March.

"Since the development of symptoms following deliberate exposure to feathers, it is probable that the reason for the symptoms at these times is due to her dressing the fowl which is eaten on these occasions. The symptoms during March can be accounted for, by the necessity of cleaning the chicken houses at that time. Also, this is the first year that the patient has kept ducks, which must be plucked every six weeks, thus accounting for the symptoms occurring during the summer time for the first time this year.

Fig. 8.—Case II. Lateral view of Fig. 6.

"November 19, 1929, occasional mild symptoms. Food diary discloses onions or chocolate as the probable cause. Has had no incapacitating bronchospasm or nasal symptoms since the experimental observation noted above.

"December 9, 1929, two deliberate exposures to feathers followed by nasal and chest symptoms. Also, suspect wheat, whole Irish potato and overdose of milk.

"December 20, 1929, nasal symptoms following exposure to wool (sewing on wool coat). Clinically better since last note which is coincidental with complete wheat avoidance.

"January 11, 1930, ate wheat (light bread) December 27, 1929, no worse.

"February 28, 1930, no further symptoms. Patient cannot be induced to return for experimental repetition of sinus filling and exposure to goose feathers."

Since that time I have observed another case in which the antral mucosa was suddenly thickened from normal proportions to a centimeter or more with definite polypoid contours, although in this case no allergen was determined (Figs. 5, 6, 7 and 8).

Still a third case was brought to my attention by Dr. J. C. Beck of Chicago in which a lipiodol injection plainly showed an almost obliterated antrum. Operation on the following morning disclosed a membrane practically normal in thickness except for a slight pouching in the vault.

CONCLUSIONS

1. The membrane lining the maxillary sinus may through allergic or other agencies vary enormously in thickness in the course of a few hours.

2. The edema may be confined to a single sinus.

3. A single x-ray examination, revealing a thickened sinus membrane, is insufficient grounds for an operation upon a sinus.

4. When seventy-two-hour plates, made for the estimation of sinus drainage, show thickening which was not perceptible on the original films, sensitivity to one of the vegetable components of the radiopaque oil employed, or to some other substance should be suspected.

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STUDIES IN ALLERGY*

I. The Specific Activity of Pollen Oil

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IT IS well recognized that substances of a nonprotein nature may be the specific excitants of hypersensitive reaction in man. Cooke in 1919 reported 15 cases of aspirin sensitivity. Coca believes that the specific allergen in the watery extracts of pollen is of nonprotein nature, but his observation has not been confirmed. Heretofore attention has been centered on the watery extracts of pollen, and the possibility that the oil present in pollen might also act as a specific allergen has apparently been overlooked.

This preliminary report will record the observations made with the oil of ragweed pollen and certain other oils.

Experiment I.—Oil was removed from dry ragweed pollen with the usual fat solvents such as toluol, carbon tetrachloride, ethyl ether and petroleum ether. The extraction may be carried out either by washing the pollen on a Seitz filter with reduced pressure, or preferably in a Soxhlet apparatus. In both procedures, using the solvents mentioned, about 12 per cent by weight of pollen is removed. After evaporation of the solvent the residue is dark, greenish-brown in color with semisolid oily consistency. In every case before testing, the oil was redissolved in a specially prepared water free solvent to exclude all water soluble material and filtered through a Seitz filter to remove pollen granules mechanically present in the oil. Qualitative chemical tests showed absence of nitrogen and phosphorus.

Tests were made with the pure oil by the scratch method. Intradermal tests were made with a suspension of oil in 1 per cent alcoholic saline solution. Control tests were made with timothy pollen oil and cottonseed oil purified and prepared in the same way.

Thirty cases with a clinical history of autumnal hay fever and found sensitive to the watery extract of ragweed pollen were tested with the oil by the scratch and intradermal method. About two-thirds of them gave positive immediate skin reactions of the characteristic urticarial type. All were negative to the watery extracts of timothy pollen and cottonseed and to the oil of timothy pollen and cottonseed. Serum from the oil sensitive cases in this group was used for passive

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transfer of sensitization by the method of Prausnitz and Küster. Sensitized sites gave positive reactions and control sites were negative.

Experiment II.—Olive oil, glycerin and petroleum were added to ragweed pollen. After standing for six hours it was separated, filtered through a Seitz filter and tested. Positive reactions were obtained on ragweed sensitive cases. As a control, olive oil, glycerin and petrolatum were added to ragweed pollen from which all oil had been removed. After extracting for seven days the solvents were filtered and tested. Reactions on ragweed sensitive cases were negative. This experiment seems to show that the allergen is naturally present in the oil and that the positive skin reactions were not due to traces of water soluble allergens.

Experiment III.—Ragweed pollen oil was taken up in petroleum ether and thoroughly washed with a small amount of saline which was then separated. Three such successive washings were done, and the saline was separately saved and filtered for testing. Positive reactions of slight degree and equal intensity were obtained with each of the three successive washings. The oil recovered after the washings showed no appreciable change in its reactions. If the active substance in the oil was really water soluble, undoubtedly the saline washings would have shown more intense reactions and the first washing would have been more active than the second or third. The presence of such slight reactions in the saline washings can best be explained by a slight solubility of the oil in water.

Experiment IV.—Oil was extracted from the separate pollens of the two prevalent varieties of ragweed—*trifida* and *artemisiaefolia*. Tests by intradermal and scratch methods on fifteen clinical cases, which had proved sensitive to watery extract, showed the same reactions to the two oils and bear out the former observations on the biologic identity of the two ragweed pollens.

Additional facts have been elicited as follows: Ragweed pollen oil apparently remains fully active after eight months at room temperature, and its activity is not impaired by heating at 125° C. for one-half hour. Oils extracted from horse and dog dander, orris, wheat and walnut have so far been negative in the few specifically sensitive cases tested. The oil of timothy pollen is specifically active in certain cases of early hay fever sensitive to the watery extract of this pollen.

It was noted in some of the cases tested with oil of ragweed pollen that a dermatitis developed at the test site five to twenty-one days later. This is probably the same reaction as that observed by Cooke* in clinical cases of seasonal dermatitis. His cases were found to react to the absolute alcohol extract of the dried leaf of the ragweed plant. He regards these cases as similar to dermatitis venenata.

*Personal communication.

SUMMARY

An important question arises as to whether the active substance in the oil is identical in its biologic reactions with that in the watery extract of pollen. The fact that but two-thirds of the cases reactive to watery extract react also to oil indicates either a quantitative or a qualitative difference in the active substance of the two extracts.

Tests on passively sensitized areas of skin in normal cases have shown activity to water extract when these sites had been exhausted by the oil extract. Further experiments along these lines are being done.

STUDIES ON THE POLLEN CONTENT OF THE AIR*

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TORONTO, CANADA

THE rôle played by pollens in the causation of hay fever and asthma has been extensively studied in the past ten or twelve years. These investigations have been productive of an enormous amount of information regarding the relationship between such pollens and the symptoms they produce. The result is that this subject is now occupying a very important part in the study of disease in general.

Since the North American continent possesses such a wealth of vegetation, it is natural that the problem of the relative importance of the various pollens produced by this vegetation should be complex. Studies made to determine the presence of hypersensitiveness in hay fever patients to pollens of a wide variety of plants, have led investigators to name a great number of species as responsible for the production of hay fever symptoms. This complexity presents a tremendous problem when it comes to the practical application of these researches, namely in determining the type of pollen to be used in treating any given case presenting symptoms of hay fever. For example, in treating a patient for hay fever occurring during the months of late August, September and early October, if one is to include, in the antigen used, the pollen of ragweed, daisy, goldenrod, cosmos, goldenglow, sunflower and aster in the belief that those plants are responsible for the symptoms of various sufferers, it is obvious that only a small quantity of each one of these can be included in the solution because the total amount will necessarily be too great. These plants all belong to the Compositae family. It has been shown that the patients will react to skin tests with pollens botanically related to the chief offender, but there may be no clinical evidence that the patient actually suffers from any but the one particular pollen. It is obvious that the inclusion of such other pollens in the extract would be superfluous and in fact would actually reduce the amount of the essential pollen in the product. Anyone who has performed tests on many patients suffering from hay fever will corroborate the observation that positive tests are obtained with pollens that are certainly not present in the environment of that patient at the time they have hay fever. In other words, it is certain that skin tests alone, unrelated to clinical observation of the individual case, are not a reliable guide as to the important pollens in any given case. It, therefore, seemed advisable to us that some studies should be made in this locality to determine what pollens contaminate the atmosphere in a representative area at any given season so as to form

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some measure of authoritative opinion as to the relative importance of the various pollens causing hay fever. It was, therefore, decided to carry out observations on the actual pollen content of the air throughout the season of pollination in this city. This has been done for a period of three years. It is felt that the result of this investigation should be put on record, particularly as the work would seem to justify the simplification of the treatment of this disease.

Numerous articles have already appeared in the literature dealing with some aspects of the general subject of pollen content in the air. Notable among these has been the work of Durham working alone and with various collaborators. Duke and Durham[1] conclude from a comparison of pollen content of the air that it is easy to explain why treatment which may be successful in one city or one year may be a failure in another city or in the same city in a different year. Koessler and Durham[2] emphasize the importance of field work to supplement examination of pollen slides. Rowe[3] in studying the air content around the east shore of San Francisco Bay found pollen throughout the year except on days of constant rain. He also confirms the conclusions of Koessler and Durham that various species of pollens are evenly distributed throughout the entire air regardless of altitude. In this connection mention may be made of the observations of Scheppegrell[4] who found pollen in the air at high altitudes as determined by exposure of slides during airplane flights. Balyeat[5] in studying the factors which determine the pollen content of the air found that rainfall plays an important part. Other factors are luxuriance of plants, profuseness with which pollen is produced by each bloom, wind velocity and sunshine. Durham[6] states that the dates of onset and close of the season in any particular place do not vary greatly from year to year. Piness and McMinn[7] present a key for the identification of pollen granules found in the air.

Clinically as well as botanically there seem to be three definite seasons for the extensive pollution of the atmosphere with large amounts of pollen in this vicinity. The first season occurs with the blooming of the trees and covers a period from late March to the end of May. The second period coincides with the pollination of the grasses and covers the months of June and July, sometimes extending into the early part of August. The third and greatest season, judging by the number of patients affected, is that of late August and the month of September and early October until the first heavy frost.

TECHNIC

The technic employed for the detection of pollen in the air was as follows:

Ordinary glass slides were coated with a thin layer of glycerin jelly prepared according to Kaiser's formula:

Finest French gelatin	40 gm.
Distilled water	2 c.c.
Glycerin	325 c.c.
Carbolic acid crystals	5 gm.

The gelatin is soaked for two hours in water, and the glycerin and carbolic acid are then added. This mixture is heated in a water-bath for from two to fifteen minutes, stirring all the time until the mixture is cooled. It is then filtered in a paraffin oven, poured into tubes and corked. Before using the jelly it is melted in a water-bath and smeared over the slide with a glass rod. Care was taken to cover only a portion of the glass slide equivalent to the surface area of the ordinary cover slip.

Slides so prepared were left exposed to the air on window ledges in various parts of the city of Toronto for a period of twenty-four hours. They were then collected and a drop of glycerin jelly was added to the surface already prepared on the slide and a cover slip mounted on this.

In such a preparation the pollen granules can usually be made out quite readily with the low dry power of the microscope. It is usually necessary, however, to use the high dry lens for definite identification of the type of pollen. If the number of pollen granules which have been caught on the slide is small, the whole area is examined, and all the granules are counted. If there are large numbers of pollen granules on the slide, it is not necessary to count the whole area but rather to count a certain definite proportion of the whole slide. A simple calculation will then suffice to indicate the approximate number on the whole slide. A mechanical stage is always used in making the counts. The information thus obtained is both qualitative and quantitative.

In order that the counts obtained shall not be misleading it is necessary to make a note of the character of the weather for the time the slide is exposed, as occasionally in spite of special care, it is impossible to prevent rains from washing some of the pollen granules off the slide. As intimated before, slide preparations were exposed on different parts of various buildings at different levels from the ground and on all sides of the buildings. The lowest exposure was just above the ground, the highest on the fourth story. Slides were exposed in downtown areas as well as in various parts of the residential areas of the city.

In conjunction with these laboratory investigations, simultaneous field observations were made to determine the pollination dates and general prevalence of the various types of vegetation in the different seasons.

THE TREE SEASON

The pollens most commonly found to be responsible for hay fever symptoms during this season were those of maple, oak, and birch. Occasionally one finds a patient who suffers from the pollen of poplar, willow, horse-chestnut, or elm.

The time of pollination was found to be remarkably constant, although if the season was advanced, the date of appearance of any given pollen might be several days earlier than the average. Similarly if the season was late, the date of appearance might be delayed a few days. This variation, however, did not prove to be as great as one would imagine. The first pollen to appear in the air is that of the silver maple. This tree begins to bloom and to contaminate the air with its pollen during the last week in March. It is closely followed by the elm and other maples, the pollens of which are almost indistinguishable on microscopic examination, so that it seems reasonable to group these together. As a matter of fact there are comparatively few patients who are sensitive to elm, so that this pollen may be disregarded. Another type of pollen which is easily confused microscopically with that of maple is that of the oak. The oak season, however, occurs during the last three weeks of May and the first week of June, whereas the maple ceases to bloom about the middle of May. It is not difficult, therefore, to obtain fairly accurate records of the amount of pollen in the air from each of these species.

The pollen of the birch is a very distinctive one, easily recognized under the microscope, especially by reason of its three germinal pores. We have found no other pollen which might be confused with this in its season. Our records show that the pollen of birch begins to appear in the first week in May and reaches its peak approximately the twenty-second day of May. By the first of June there is very little remaining, although occasional pollen granules are found on into the month of June.

The poplar trees produce a large amount of pollen, but this does not cause hay fever in many people. These trees begin to bloom about the last week in April and the first week or two in May.

Willow is only an occasional cause of hay fever. It pollinates during the latter part of April and early in May. Our studies of the pollen content of the air in this city did not reveal any willow on our slides.

Horse-chestnut blooms during the last two weeks of May and the first week in June. Its pollen is very abundant, but it has not been shown to be a prolific cause of hay fever. The pollen granules are very distinctive and easily recognized and identified.

Following is a description of the pollens of the various trees which occur in large numbers in this vicinity. This is included because it would seem advantageous to describe the appearance of such pollens when collected on the particular medium which was used.

MAPLE:

Size: 26 to 29 microns.
Color: Very pale yellow.
Extine is clear, moderately thick with a coarsely granular perin.

ELM:

Size: 24 to 28 microns.

Color: Very pale yellow.

Shape: Round and fairly regular.

Extine is clear and thick and the perin coarsely granulated. It is difficult to distinguish this pollen from that of the maple. The perin is thicker, and the size on the whole is slightly smaller, but these characteristics are not sufficient to make a definite differentiation possible.

POPLAR:

Size: 24 to 26 microns.

Color: Pale yellow.

Shape: Round with a thick clear extine and coarsely granulated perin. This pollen, as well as that of the elm, has a much shorter season than the maple with which it is easily confused. In these parts it is not nearly so important as the maple in the production of hay fever symptoms. It ranks with the elm as one of the less important of trees.

WILLOW:

Size: 14 to 17 microns.

Color: Fairly pale yellow.

Shape: Round.

Fairly thick and clear smooth extine. The perin is homogeneous.

BIRCH:

This is a very easily identified pollen granule.

Size: 24 to 28 microns.

Color: Definitely yellow.

Narrow yellow extine.

Very finely granulated perin. It always occurs with three distinct germinal pores, two of which are often in focus at the same time. In general this pollen has a very definite, regular, and clear-cut appearance.

CHESTNUT:

Size: 17 to 21 microns.

Shape: Slightly oval.

Smooth thin extine and homogeneous perin.

Occasionally they have a pale brick-red color but usually they are colorless. These pollen granules are easily recognized.

OAK:

Size: 26 to 28 microns.

Color: Yellow (pale).

Shape: Round.

The extine is thick and clear.

The perin is coarsely granular.

This pollen is difficult to distinguish from elm, maple, and poplar, but may be recognized because of its later season and because many of the pollen granules, as they mature, develop three equally spaced germinal pores, which, while not as definite as the pores of the birch, are fairly characteristic.

Figs. 1 and 2 are composite charts showing the prevalence of the pollens indicated during the years 1928 and 1929. They serve to show in a graphic manner the relative amounts of pollen in the air on the dates indicated.

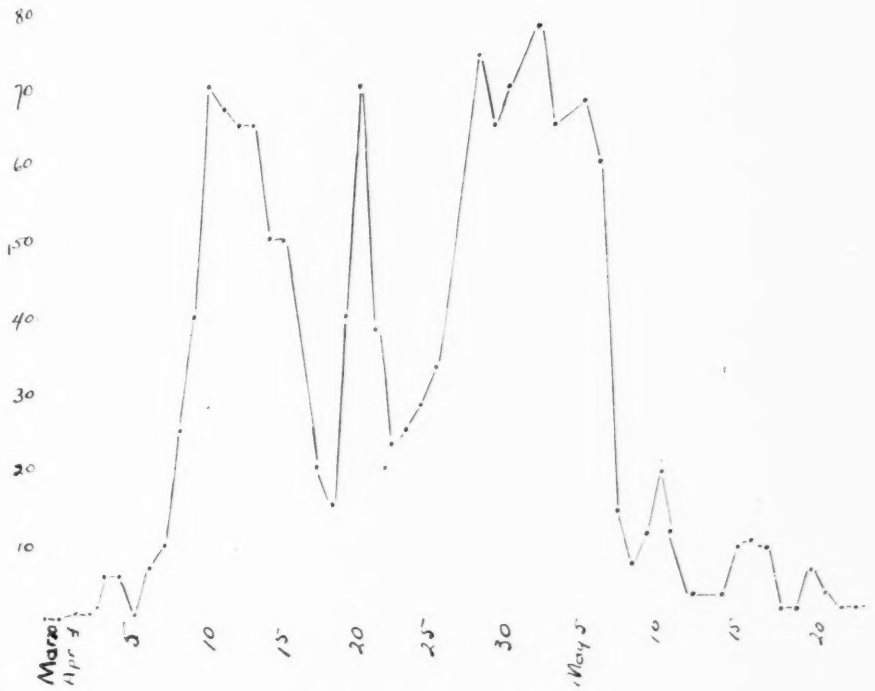

Fig. 1.—Maple, elm, oak, 1928-1929.

THE GRASS SEASON

About 10 per cent of all patients suffering from hay fever develop their symptoms during the season of June and July. Since the onset of their symptoms coincides roughly with the blooming of roses this form of hay fever is very commonly called rose fever, and it is sometimes difficult to persuade these patients that roses are not the cause of their trouble. In a fairly extensive practice during the past nine years I have not encountered a single rose case, unless we include in this group those who have symptoms on close contact with roses. Such cases invariably will have the major portion of their symptoms from grass pollens and therefore can hardly be classed as rose cases.

Similarly this season is the flowering season for daisies as well as sheep sorrel. The pollens of both of these plants have frequently been blamed for the production of important hay fever symptoms. I have not a single case of hay fever due to these pollens, although I have a number of patients who react when tested with them. Particularly is this true of daisy.

Our studies of the pollen content of the air during June and July make clear the reason why we do not find clinical cases of hay fever in this district due to these pollens. We found that practically the only pollen granules which appeared on our slides were those of the grasses, even though there were numerous flowers including daisies

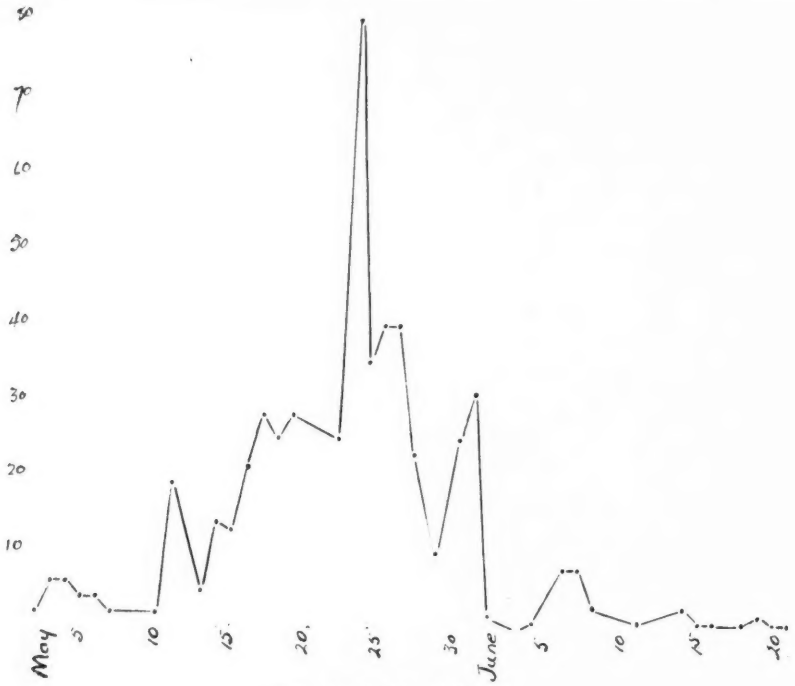

Fig. 2.—Birch, 1928-1929.

blooming in the vicinity of the buildings on which these slides were exposed. The absence of pollen other than that of grass in the air may best be explained by the fact, as botanists have long since pointed out, that bright flowers are insect pollinated and therefore have heavy pollens which do not get up into the air and therefore cannot be an important cause of hay fever.

The grass season is ushered in as a rule the first week in June by the pollination of June grass, commonly called Kentucky blue grass. Occasionally this grass blooms in sunny exposed places as early as the twenty-fourth of May. The pollination season for this species continues throughout the month of June. The field studies of this plant, coinci-

dent with a pollen slide as described, show that the presence of this pollen in the air in large quantities corresponds fairly well with its great prevalence throughout the country. The appearance of the granules on the slides occurs three or four days after blooming is observed in the field.

Approximately one week later orchard grass usually makes its appearance on the slides, and here again field studies show that this is a very accurate measure of the prevalence of this plant. While the pollen of orchard grass is somewhat larger than that of June grass on the average, there is not sufficient difference to make it possible to differentiate these two pollens with accuracy on the slides. Under these circumstances the field studies showing the prevalence of the grasses in various parts of the community are of the very greatest importance in determining the rôle played by the respective pollens. Orchard grass completes its pollination about the last week in June.

About the first of July timothy pollen appears in the air. Fortunately, the pollen of this grass is considerably larger than any of the others and consequently is easily recognized. The appearance of the pollen granule of timothy coincides quite accurately with the field studies showing the blooming of this grass. Timothy is principally grown in this community on outlying farms but also is very prevalent in waste land within the city.

About a week later than timothy and bearing about the same relation to it that orchard grass does to June grass, red top makes its appearance on the slides. Here again it is not difficult to recognize the pollen because of its comparatively small size, the diameter averaging from 24 to 27 microns, whereas timothy measures between 35 to 38 microns in diameter. The pollination season for timothy and red top lasts throughout the month of July, the last week of which it tapers off considerably. Figs. 3 and 4 illustrate the prevalence of these pollens during the seasons of 1927-1928. In these charts there appears to be a slight lag in the appearance of the pollen on the slides as compared with field studies showing the blooming of the plant. Thus the average date for finding pollen of June grass was June 11, whereas there are certain localities where on a southern slope the June grass may be in bloom as early as May. Similarly the charts show a small amount of pollen in the atmosphere in the early part of August. This is accounted for by the fact that the granules may be blown about for a certain period of time after the plants have ceased producing new pollen.

There are, of course, other grasses which appear in this vicinity, but these do not seem to be present in large enough numbers to warrant very serious consideration from the standpoint of hay fever. These grasses include meadow foxtail, sweet vernal, ray grass, and others.

Following is a description of the pollen grains of the four important grasses.

JUNE GRASS:

Size: 27 to 30 microns in diameter.
Colorless.
Shape: Perfectly round with a smooth refractile outline.
Extine: Very narrow, clear and colorless.
Perin: Finely granulated.

ORCHARD GRASS:

Size: 27 to 25 microns in diameter.
Colorless.
Shape: Perfectly round and smooth.
Extine: Narrow, clear and refractile.
Perin: Finely granulated.

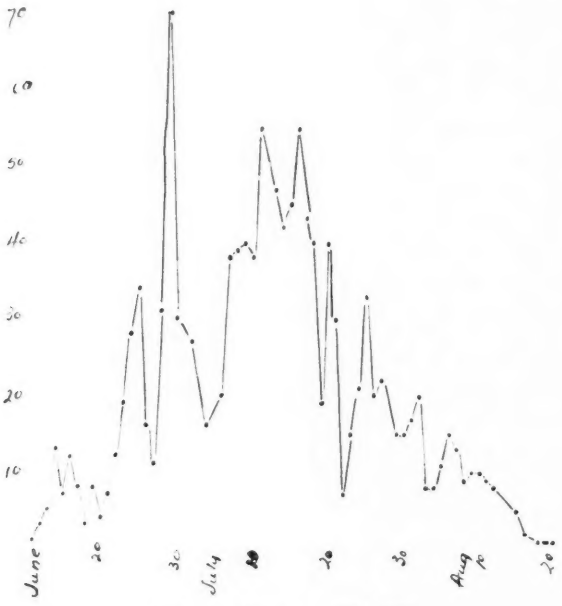

Fig. 3.—Grasses, 1928-1929.

TIMOTHY:

Size: 35 to 38 microns in diameter.
Colorless.
Shape: Round and smooth with refractile surface.
Extine: Narrow, clear, and colorless.
Perin: Finely granulated.

RED TOP:

Size: 24 to 27 microns in diameter.
Color: Almost colorless.
Shape: Round, smooth.
Extine: Clear, thin and highiy refractile.
Perin: Finely granulated.

Fig. 3 is a composite chart including all four grasses and represents the atmospheric content for the years 1928 and 1929. It reflects with remarkable accuracy the severity and durations of symptoms complained of by the sufferers from hay fever during the grass season.

AUTUMNAL HAY FEVER

We now come to the third hay fever season of the year, namely the season beginning about the middle of August and extending to the heavy frost. Here again, many pollens have been held responsible for the characteristic symptoms during this period of the year. Those most commonly believed to be the usual causes of symptoms are ragweed, goldenrod, daisy, cosmos, asters, sunflowers, goldenglow, pigweed, and garden flowers of the sunflower group.

Fortunately the pollen slides which we exposed during this season were placed in the vicinity of most of these plants. The perennial borders of the gardens at the Toronto General Hospital are close to the Pathology Building and therefore would be expected to contribute pollen to the air in that vicinity. It is interesting to note that pollens of this sort were practically negligible in our microscopic examination of those slides. Almost all the pollen was of the ragweed type. The microscopic appearance of ragweed is not unlike that of goldenrod. These are the only pollens of the whole group that are likely to be confused one with the other. We have made careful studies of many preparations of both these pollens and feel able to differentiate between them. The main point of difference is the greater length of the spicules of the surface of the goldenrod pollen grain. These spicules are not only longer but sharper than those of the ragweed pollen grain. To the inexperienced these differences may appear very slight, but one soon comes to recognize them readily on careful examination.

A glance at Fig. 4 will show that ragweed accounts for practically all the hay fever of this season of the year. We are convinced of this not only by the pollen content of our slides, but also by the fact that the symptoms of a patient at this time of the year coincide in their onset and in the cessation with the pollination season of ragweed. Ragweed begins to bloom about the fifteenth of August, whereas goldenrod is usually in bloom from the first of August. Practically none of these patients complain of symptoms during the first half of the month but almost universally mention any date from the fifteenth to the twentieth or later as the date of the onset of their hay fever.

While it is true that many of these patients will react in the cutaneous tests to pollens of many of the plants mentioned above as being held responsible for hay fever at this season, these patients almost without exception will not have hay fever from them unless they are in close contact with such flowers. That is to say, if they remain out of the garden and refrain from having bouquets of flowers in the house, pollen

of these sources will fail to cause symptoms. The difficulty with ragweed is that since it is able to travel in the air for as much as ten miles or more, it is impossible for sensitive patients to escape from it unless they are able to live in the region where ragweed is unknown. This fact, to my mind, is conclusive evidence of the all-importance of ragweed. Many of these sufferers have experienced relief from their symptoms when they go to the British Isles or anywhere in Europe. It is well known, of course, that all the various flowers mentioned bloom in these countries, but ragweed is unknown there. Fall hay fever is not encountered in England, and physicians there refer to it as "American hay fever."

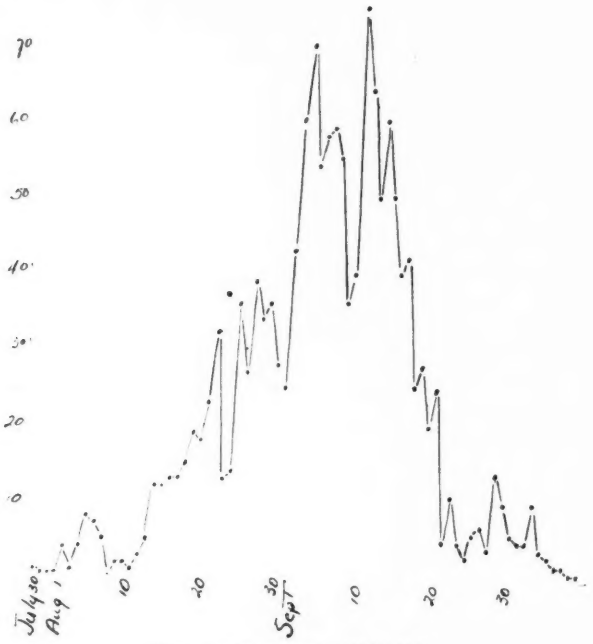

Fig. 4.—Ragweed, 1928-1929.

Following is a description of the pollen grains of ragweed and goldenrod.

RAGWEED:

Size: 17 to 20 microns.

Color: Pale yellow.

Shape: Round, narrow extine. Surface covered with short blunt spicules causing the pollen grain to resemble a golf ball in appearance.

GOLDENROD:

Size: 17 to 20 microns.

Color: Pale yellow.

Shape: Round, narrow extine. Surface covered with sharp spicules which are slenderer and longer than those of ragweed.

Fig. 4 represents the average atmospheric pollen content of the seasons of 1928 and 1929. This is exclusively ragweed.

SUMMARY

Attention is called to the possibility of simplifying the specific treatment of hay fever by studies on the pollen content of the air.

Such studies have shown that the pollen contamination of the air is not as complex as is commonly supposed. It is pointed out that not a few individuals suffering from hay fever show a positive skin reaction to pollens which are not found in the air apart from that in close proximity to the flowers concerned. It follows, therefore, that skin tests alone are not necessarily a reliable guide in determining the pollens to be used for specific therapy in any individual case. Skin tests should be interpreted in the light of studies of the pollen content of the air as reported in this paper.

The technic for such a study is outlined, and the general characteristics of the various pollen grains are described. The results of observations in Toronto are recorded.

In the tree season the pollen of maple, elm, oak, and birch seem to be more important than that of other species. Of the grasses, timothy, red top, June grass, and orchard grass appear to cause practically all the hay fever during their pollination season. In the autumn type ragweed is recovered almost inclusively, and it would seem logical from this observation and for reasons mentioned earlier in this paper to blame this plant for the vast amount of suffering from hay fever and hay asthma during August and September.

It would appear reasonable to simplify the specific treatment of the various types of hay fever in accordance with the findings recorded above.

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BOXWOOD SENSITIVENESS*

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SENSITIVENESS to wood in general is mentioned very little in the literature.

Bahn[1] reported a case of asthma due to pine wood in a worker in a sawmill; he quoted 7 other cases reported in 1921 by Gade and Curshman in workers in sawmills which were diagnosed as due to pneumoconiosis, their allergic basis not being suspected.

Longin[2] described anaphylactic skin eruptions caused by freshly cut wood.

In the present report, I wish to describe an instance of bronchial asthma due to boxwood sensitiveness.

A man thirty-four years old, watchmaker by trade for the past fifteen years, came to me on July 15, 1929, with the following history: About five years ago he began to experience a tickling sensation in his throat and within three or four months he developed a steady cough with a sense of constriction in the larynx. At the end of one year he began to have mild attacks of dyspnea at fortnightly intervals, lasting from one-half to one hour. Later, these attacks began to recur at more frequent intervals, becoming severer in character and of longer duration, necessitating him to stay away from work for a few days every week. While away from work he felt entirely relieved. His condition steadily grew worse so that for the last two years he could no longer keep up his work regularly. He changed from one jeweler to another without relief. The history suggested something environmental in his occupation as a causative factor in producing his attacks and accordingly he was asked to bring samples of materials used at work. In the meantime, all common proteins tested gave no reaction.

He was tested with sawdust, employed in cleaning gold, by the scratch method. This gave a very marked positive skin reaction characterized by an enormous ameboid wheal 5 cm. in diameter and surrounded by a marked zone of erythema. He was then tested with commercial boxwood and gave a more marked positive reaction.

When the etiologic factor was thus established and the patient informed of the nature of it, he could then readily associate his great discomfort with those times when he came near the sawdust box. While he was in my office, I placed the sample of sawdust near him in an open dish and within ten or fifteen minutes he began to experience a sense of constriction in his chest and the same evening he had a moderately severe attack of asthma.

Having thus confirmed the clinical history with the positive skin findings, I next proceeded with the passive transfer of his hypersensitiveness to normal skin, according to the method of Prausnitz and Küstner. For this purpose I sensitized three sites on the arm and forearm of six normal nonallergic individuals. The antigen used for the intradermal test was a boxwood extract prepared by Coca's

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method, using extracting fluid No. 2 as for pollens. For the scratch method the samples of sawdust and boxwood were used. The tests were made at intervals of twenty-four, forty-eight, and seventy-two hours on two patients at each interval, the nonsensitized arm being used as a control.

Table I shows the result of the passive transfer of hypersensitiveness.

TABLE I

INTERVAL	PERSONS	BOXWOOD EXTRACT INTRACUTANEOUS	BOXWOOD POWDER CUTANEOUS	SAWDUST SAMPLE CUTANEOUS	CONTROL
24 hr.	1	+++	++	+	0
	2	+++	++	+	0
48 hr.	3	++++	+++	++	0
	4	++++	+++	++	0
72 hr.	5	+++	++	++	0
	6	+++	++	++	0

Boxwood [Box; Evergreen Box; Buxus (Buxus Sempervirens); (Fam. Buxaceoe)] is a slow growing evergreen shrub, frequently attaining the size of a small tree. It is a native of southern parts of Europe and western Asia, and is frequently cultivated in this country as an ornamental plant. The wood is very hard and close-grained and is in great demand for engraving and finer turnery work. As sawdust, it is used extensively by jewelers for drying and cleansing gold immersed in various cleansing fluids. An alkaloid buxine which has been discovered in the leaves of the tree is identical with bebeerine of Nectendara Bark; and a second alkaloid, parabuxine, was found by Pavia to accompany buxine. Formerly, it was used as a febrifuge, tonic, and antiperiodic, but is little employed in medicine today.

A chemical analysis of sawdust was made by extracting one portion with distilled water and another with 5 per cent sodium bicarbonate solution as follows: the sawdust was extracted with distilled water several times and each time it yielded a dark brown solution. These solutions were combined and, on drying, a dark brown sticky mass was obtained. This material was then redissolved in water and dialyzed. The dialysate was tested on the patient by the scratch method and found to be positive with a strong reaction. Both the original solution and the dialysate were then dried and tested in crystal form. These gave similar positive reactions. The same procedure was followed with the alkaline extract, and the same results were obtained in testing the patient; the reactions, however, being somewhat stronger.

Some of each of the solutions were treated with solid ammonium hydroxide, but failed to yield any precipitate. The protein color tests were negative with the exception of the Xanthoproteic test which was very faintly positive.

Two other samples of sawdust from hard and soft wood obtained from a neighboring mill gave negative skin tests and no symptoms on direct inhalation.

The management of the patient consisted partly in advising prophylaxis; i.e., to avoid contact as much as possible with the offending agent. This necessitated finding a small jewelry shop where little sawdust was used. In addition, a specific course of desensitization with boxwood extract prepared by extraction with Coca's extracting fluid No. 2, having a nitrogen content of 6.8 mg. was started. On a preliminary test with this extract intradermally, less than one drop gave a very marked immediate local reaction with marked tenderness and heat. A delayed constitutional reaction characterized by a slight headache, rise of temperature, and an enormous swelling of the arm and forearm with an erythema reaching 6 or 7 cm. in diameter at the site of injection, resulted.

Because the extract was very potent it was diluted 10 times, thus obtaining a nitrogen content of 0.68, and Table II shows the result of treatment with this extract.

TABLE II

7/27/29	0.05 c.c.	Reaction—Enormous swelling of arm for 72 hr. Mild asthmatic attack.
8/10/29	0.1 "	" Dyspneic for 3 hr. after injection.
8/14/29	0.1 "	" Substernal tightness. Local reaction.
8/20/29	0.05 "	None
8/24/29	0.1 "	"
8/27/29	0.15 "	"
8/31/29	0.25 "	"
9/10/29	0.15 "	"
9/14/29	0.2 "	"
9/21/29	0.25 "	"
9/28/29	0.35 "	"

When the patient's condition improved to the point where there were no attacks, he was told to come back in six weeks for retesting. On November 19, he was retested with boxwood as before and gave a three plus (+++) reaction with all three antigens. A passive transfer was made and this also gave a three plus (+++) reaction.

Clinically, however, his condition is excellent. He works in a small jewelry shop, and uses a somewhat different grade of sawdust which is kept in a closed container, although he reacts to this on skin testing. He gained considerable weight and did not have a single cold this winter, whereas last year he had an attack of bronchitis of five weeks' duration.

CONCLUSION

This case appears to be one of acquired specific sensitiveness to boxwood. There is no history of allergy in childhood nor in the family. Desensitization was not successful, since seven weeks after

treatment he showed no lessened skin reactivity on retesting, nor was there a diminution of reagins in his blood, as seen from the second passive transfer series. However, during the process of desensitization a gradual tolerance to boxwood was established, and clinically there is freedom from any symptoms of bronchial asthma.

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FOOD ALLERGY AND NASAL SYMPTOMS*

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IN A PREVIOUS communication,[1] it was stated that, at times, the ingestion of food induced nasal symptoms. This had been demonstrated by excluding from the diet either the suspected food or the food to which a positive cutaneous reaction had been obtained. When the nasal symptoms had subsided, an endeavor to reproduce these symptoms by deliberately feeding the suspected or the reacting food was made. In this manner, it was possible to demonstrate that nasal symptoms would follow the ingestion of specific foods in a group of thirty-three cases of allergy. Since the foregoing report, additional cases of allergy have been studied in like manner. It is now possible to report the data obtained from a somewhat larger series of cases of this type.

The present series consists of a total of ninety-five cases in which it was possible to induce an allergic nasal reaction by ingestion. Of these there are nineteen cases of hay fever, thirteen of hay fever with bronchial asthma, forty-two of perennial vasomotor rhinitis, twelve of perennial vasomotor rhinitis with bronchial asthma, and nine cases of allergy in which the chief complaint was other than nasal, such as headaches, abdominal pain, angioneurotic edema, mucous colitis, but in which nasal symptoms were nevertheless present.

From each of these cases there was developed an exhaustive detailed clinical history dealing with the presenting symptom, the antecedents, the environment and the diet. Allergic tests were done with the usual inhalants and food allergens by both the intradermal and the cut method; the cut method being employed, as a rule, to test with the infrequent factors such as cucumber, mint, cantaloupe, ginger. In addition, a dietetic diary was kept of all foods eaten, and this was studied in relation to symptoms as they developed from time to time. In each case, foods giving positive cutaneous tests and those suspected from a study of the food diary were excluded from the diet. When the patient became symptom free, deliberate feedings of the suspected food were instituted. If nasal symptoms followed, this observation was checked, and rechecked, by deliberate feedings.

As the result of deliberate feedings, it was found that eight cases were sensitive to only one food, and eighty-seven cases were sensitive

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to more than one food. In one of the singly sensitive cases, positive reactions were obtained by the intradermal method to egg, tomato and orange; but only with the ingestion of egg did vasomotor rhinitis develop. As the result of cutaneous tests by both the intradermal and the cut method, eighty-nine cases of this series were found sensitive. Tests were reported as positive when they persistently differed from the control tests. Reactions ordinarily recorded as plus minus or one plus were considered positive in this study, which accounts for the large number of positive reactions reported. This was done deliberately because these slight reactions were considered of possible significance and because it was not known where else to draw the line between positive and negative reactions. It was found that some foods which gave suspiciously positive skin tests induced no symptoms, while in some cases, these doubtful tests were of decided significance. There were six individuals in whom it was impossible to obtain positive cutaneous reactions on the upper arm by the intradermal method, or on the forearm by the cut method; three of these were relieved by avoiding one food in their diet; the others were found sensitive to more than one food.

When considering the series as a whole, wheat was found the most frequent factor. This was responsible for symptoms in thirty instances. Then, in sequence, followed egg (twenty-four instances), milk (seventeen instances), chocolate (fifteen instances), potato (eleven instances), string bean (twelve instances) and other foods in considerably smaller number. Fruits, as a group, accounted for twenty-four instances; but these were somewhat widely distributed among thirteen fruits, although for six of these cantaloupe was responsible. (Table I.) It is noteworthy that wheat is the most frequent factor in all clinical types of nasal allergy and that chocolate, string bean and fruit are often the offending allergens in the perennial vasomotor rhinitis group.

In the previous communication, examples were given of cases of hay fever wherein the symptoms seemed to be induced or influenced by the ingestion of food. It was also observed that some of these cases of hay fever were entirely controlled during the season of pollination by food avoidance alone. In the present series, nineteen cases are classified as hay fever cases because this was their chief complaint. However, in addition to giving cutaneous reactions to pollen, all of these gave reactions to foods, and seven of them gave reactions to inhalants other than pollens. The clinical results in these nineteen cases with particular reference to the influence of allergens other than pollen, were as follows:

Five (one observed one year, two for two years, one for three years, and one for five years) have never received pollen injections and have obtained excellent relief by avoidance of the suspected foods and in-

TABLE I

FOODS RESPONSIBLE FOR NASAL ALLERGY IN THE CASES REPORTED

	HAY FEVER	HAY FEVER AND ASTHMA	PERENNIAL VASOMOTOR RHINITIS	PERENNIAL VASOMOTOR RHINITIS AND ASTHMA	OTHER ALLERGIC MANIFESTATIONS WITH NASAL SYMPTOMS	TOTAL
Wheat	5	2	14	3	6	30
Egg	4	2	14	2	2	24
Milk	2	1	6	3	5	17
Chocolate	1	1	9	1	3	15
String bean	4	3	5			12
Potato		4	3	4		11
Pea	2	2	2	2	1	9
Salmon	1	2	2	3		8
Tomato	1	1	4		1	7
Onion			3	1	2	6
Cantaloupe		3	1	2		6
Beef	1	1	4			6
Corn	1		2	1	1	5
Pecan		1	3	1		5
Asparagus		1	1	1	1	4
Apple	1		3			4
Grape		1	1		1	3
Peanut	1	1		1		3
Pork		1	2			3
Spinach	1	1		1		3
Almonds	2		1			3
Peach			2			2
Strawberry	1			1		2
Watermelon			2			2
Sweet potato				1	1	2
Chicken		1	1			2
Cabbage	1		1			2
Cucumber	1	1				2
Rice	1		1			2
Cherry			1			1
Raspberry			1			1
Blackberry			1			1
Pineapple			1			1
Grapefruit		1				1
Orange			1			1
Ginger		1				1
Green pepper			1			1
Lettuce					1	1
Lima bean				1		1
Radish				1		1
Garlic			1			1
Rye			1			1
Veal			1			1
Walnut			1			1
Rhubarb				1		1
Chicory			1			1
Mint					1	1
Carrot	1					1
Oat			1			1

halants (nonpollen). In addition, one case observed for six years was treated by pollen injections combined with food and inhalant avoidance for the first four seasons and obtained complete relief. For the next two seasons, treatment was by food and inhalant avoidance alone, and again complete relief followed. Another case, observed for three

years, had pollen injections combined with food and inhalant avoidance the first season obtaining 100 per cent relief, and obtained 80 per cent plus relief through the second and third seasons by diet alone.

Six cases have been treated by pollen injections combined with diet. One observed for two seasons, obtained less than 50 per cent benefit. Another case, seen through one season, also obtained less than 50 per cent relief. Residence at school, in this case, very probably prevented accurate observance of dietetic restrictions. One, with only dietary restrictions for the first year, obtained no benefit but did obtain 80 per cent relief, during the second season, as the result of dietary restrictions and pollen injections up to 0.15 c.c. of a 1 to 100 dilution. The three remaining cases of this group obtained better than 80 per cent relief by injections and restrictions. Of the six remaining cases of the hay fever group, it was impossible to make any observation as to the influence of food on their seasonal symptoms.

In the hay fever with asthma group, observations on three patients have been made relative to treatment only by food restrictions. One patient was observed through two seasons. The first season, treatment by pollen injections up to 0.30 c.c. of a 1 to 1000 dilution and food restrictions resulted in neither hay fever nor asthma. The second season treated only by food restrictions also resulted in neither hay fever nor asthma. The second case, observed through two seasons, with food restrictions as the only treatment, obtained 80 per cent relief. The third case, observed through two seasons, treated only by specific food and inhalant avoidance, had no symptoms during the first season and but one mild asthmatic attack during the second season. (Table II.)

TABLE II

RESULTS OF TREATMENT OF CASES OF HAY FEVER WITH DIET AND WITH INHALANT (NONPOLLEN) AVOIDANCE

HAY FEVER		*Therapeutic Result*
No pollen desensitization injections: food or food and inhalant avoidance only.	5 cases	80% relief
Pollen injections and food restrictions, 4 years. Food restrictions only, 2 years.	1 case	100% relief
Pollen injections and food restrictions, 1 year. Food restrictions only, 2 years	1 case	80% relief
Pollen injections and diet.	6 cases	2 less than 50% relief 4 more than 80% relief
No observations as to influence of food on symptoms.	6 cases	

HAY FEVER WITH ASTHMA		*Therapeutic Result*
Pollen injections and food restrictions 1 year. Only food restrictions, 1 year.	1 case	100% relief, both seasons
Food restrictions only, observed through 2 years.	2 cases	80% relief

These observations on pollinosis cases suggested that in order to produce symptoms, simultaneous or sequential action of several allergens was necessary, or possibly that it was a matter of total allergic dose which actually controlled the appearance and possibly, also, the severity of the symptoms. If this mechanism occurs in cases of pollinosis, it may also be present in individuals who appear to be sensitive particularly to epidermal allergens. The opportunity to make this observation was presented by the following case:

A woman, aged twenty-five years, seen March 13, 1928, complained of sneezing, nasal blocking and discharge when about horses. She also had similar nasal symptoms (not associated with horse contact) at various times throughout the year, perhaps more frequently during the spring and summer. These latter were considered as "colds" by the patient. She had had one severe attack of urticaria, presumed to be due to eating an excessive amount of fish. The maternal grandmother, who had had bronchial asthma and urticaria, was the only member of the family with evidence of allergy. Cutaneous tests by the intradermal method gave definite positive reactions to beef, wheat, rye, barley, fish and spinach (in the order of their intensity) and by the cut method, reactions to horse dander, cat epithelium, ragweed pollen and string beans were obtained.

By means of deliberate feedings, it seemed that beef when eaten in large amounts was the only food that was invariably followed by nasal blocking and coryza, sometimes with and sometimes without sneezing. Deliberate exposure to horses was then tried while the patient was on a diet without beef and no nasal symptoms developed. Many observations of this nature were made. It seemed proved that this patient had no nasal symptoms upon exposure to horses when on a beef-free diet. It is impossible to state with accuracy, whether there were more symptoms on contact with horses than from beef ingestion without horse contact. The patient thought, however, that contact with horses combined with the eating of beef was followed by more severe symptoms for a longer period than could be induced by any other procedure.

It would appear that this is an example of epidermal and food sensitization analogous to cases of food and pollen sensitization. In each of these it seems to be possible to induce nasal symptoms by food and that these symptoms are then accentuated by inhalant contact. However, the induction of nasal symptoms in these cases by the inhalant factor alone, may be dependent upon excessive exposure.

Of the patients with perennial vasomotor rhinitis, thirty-seven gave positive cutaneous reactions; twenty-five to inhalants and foods and twelve only to foods. In this group, there were also five individuals in whom no positive skin tests could be obtained; four of these were determined by deliberate feedings to be sensitive to foods, and one to food and inhalants. Of the twenty-five individuals reacting to the

inhalants and foods, thirteen gave positive skin reactions to pollen as a part of their inhalant sensitivity. The clinical experiences with cases of pollenosis led us to observe these cases through the respective periods of pollination without pollen desensitization injections. While on a diet or diet and inhalant restrictions, three of these had an increase of symptoms during the pollen season, and in ten cases pollination had no apparent influence on their symptoms. Whether these would have had symptoms, had they not been on such restrictions, is purely conjectural. Our experience with cases of pollinosis, in which the symptoms were influenced by food restrictions leads us to believe that the total allergic dose is also operative in this clinical type of allergy. Except for the three cases whose symptoms were increased during the periods of pollination (who then in the following years had pollen injections) none of these patients were given desensitization injections.

Of the patients with perennial vasomotor rhinitis and asthma, eleven gave positive cutaneous reactions to food and inhalants. In all these the sensitivity to inhalants was both to pollen and to epidermal allergens, usually feathers and orris root. In one, no positive cutaneous tests were obtained, and here the ingestion of food was determined to be the etiologic factor. Of these eleven patients who gave positive reactions to pollen, in six it appeared that pollination had no cumulative influence on their symptoms. In these cases (three observed for two years, two observed for one year, and one observed for four years) no pollen injections were administered, and their comfort was entirely controlled by avoidance of the other allergic factors. In the remaining five cases of this group, there was an increase of symptoms corresponding to the pollination of the respective plants which gave positive cutaneous reactions, but in three of these the symptoms were so mild that pollen injections were not required in the subsequent years.

In the nine cases in which the nasal symptoms were not the presenting symptoms, there were six cases of abdominal pain, one case of colitis, one case with periarticular pain, and one case of migrainoid headache. In these, the nasal symptoms commonly had been termed sinus disease, and had been thought to be the etiological factor for the presenting symptom; yet deliberate feedings, in these cases, resulted either in inducing the presenting symptoms or nasal symptoms, many times sequentially, usually the nasal symptoms being followed by the associated manifestations. In this group, multiple sensitization prevailed, both as to food and inhalants; in only one case (that of abdominal pain and nasal symptoms) were foods solely responsible for the symptoms.

Study of this series of cases indicates that multiple sensitivity is found the rule rather than the exception. From the clinical observations herewith reported it can be inferred that multiple sensitivity is responsible for the severity, the duration and quite possibly also the

initiation of symptoms. It would appear, also, that the positive skin tests are not an infallible therapeutic guide. While this study quite obviously deals with a group inadequate to yield a statistical conclusion, it emphasizes the fact that in many seasonal and nonseasonal cases of vasomotor rhinitis the symptoms are dependent upon the concomitant or upon the sequential action of several allergens.

CONCLUSIONS

1. The allergens appearing most frequently in the diet are the ones that most frequently cause the various clinical types of nasal allergy.
2. Some cases of pollinosis may be rendered comfortable merely by food restrictions.
3. Many cases of perennial vasomotor rhinitis may secure satisfactory clinical results without desensitization injections.
4. Before determining that pollen injections are imperative, one should critically consider the clinical influence of foods and inhalants other than pollen. Observation through a season of pollination not infrequently will show that such injections are unnecessary, provided other allergic factors are properly controlled.
5. In many of these cases, it would appear that the intensity or the duration and possibly also the initiation of symptoms depend upon the total allergic dose.

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THE SYMPATHETIC COMPONENT OF THE EXTRINSIC NERVE INNERVATION OF THE LUNGS IN STATUS ASTHMATICUS*

Case Report of Blocking by Alcohol Injections

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In 1912, Dixon and Ransom[1] produced bronchoconstriction in cats by stimulating the cervical sympathetic system. In 1927, Braeucker[2] also did this in the dog, and he gave as one theory for the beneficial effects produced by sympathetic interruption in the treatment of asthma, that bronchoconstrictor fibers may run in the sympathetic chain as well as in the vagus. Kuntz[3] states that vagus stimulation occasionally elicits bronchodilatation, and that these conflicting results occur only in those cases where there are some sympathetic fibers incorporated in the vagus, and some vagus fibers in the cervical sympathetic.

Papiliar and Cruceanu[4] found a decrease in respiratory volume of 50 per cent in animals during the first eight to ten days following cervical sympathectomy, or painting the ganglia with 1 per cent nicotine. Weber[5] showed that bronchoconstriction by pilocarpine was prevented only after section of both vagi and cervical cords. Fründ[6] expressed the opinion that the vagus and sympathetic represented parts of the same vegetative nervous system which is divided into tracts by more or less casual considerations, and that one or the other may carry the principal mass of tonic-stimulating fibers. Kaess, Glaser, Hesse, Jungman, Bruning, Witzel, and others, have assumed that the sympathetic is afferent and the vagus efferent.

Phillips and Scott[7] in a recent admirable review of the surgical procedures used for the relief of asthma, declare that there is a preponderance of opinion in favor of the vagus being the main bronchomotor nerve, and that there is also ample evidence that there are bronchostenotic fibers in the sympathetic.

Kümmel[8] in 1923 did a unilateral sympathectomy for asthma. He also removed the cervical sympathetics including the stellate ganglion. Braeucker[2] in 1925-1926 found that stimulating the vagus or sympathetic caused "increased resistance" to the exchange of air. He also removed sympathetic pulmonary fibers to the lungs as low as the fourth thoracic region. Leriche and Fontaine[9] in 1928 decided that it is only necessary to remove the stellate ganglion, and suggested a thoracic attack on the sympathetic.

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In several instances, bilateral cervical sympathectomy has been done. Kappis[10] in 1924 reported encouraging results from vagotomy on the right side below the point of emergence of the recurrent laryngeal nerve, and in a preliminary report declared to have obtained some good results. Daniélopolu[11] planned an extensive interruption of the fibers to the stellate ganglion, while this structure was preserved. Kümmel in 1926 reported isolation and section of the posterior pulmonary rami in asthmatic patients.

Phillips and Scott[7] conclude that "if interruption of either the sympathetic or vagus nerve is sometimes curative, sometimes ineffective, but frequently partially beneficial, then it seems reasonable that to combine these procedures may result in greater improvement than is obtained from either one alone." They report a case where both systems were severed at the posterior pulmonary plexus on the right side. The operation was quite extensive, the patient developing a hemopneumothorax.

We have come to conclusions similar to theirs regarding the surgical intervention of the sympathetic and vagus systems. We believe, however, that similar results may be obtained by blocking these systems with alcohol. The simple procedure of an injection is certainly less formidable than an extensive open operation.

The method of the intratracheal approach to the blocking of the sympathetic and vagus systems at the posterior pulmonary plexus by alcohol injection, is now in print, as well as the description of a specially devised instrument for such a procedure, designed by one of us (E. L. S.).

That the sympathetic component of the extrinsic nerve supply of the lungs is bronchodilator in character, is a belief long held by many. Kuntz[3] states that "the bronchodilator fibers are sympathetic, and arise mainly in the inferior cervical and first thoracic ganglia. The preganglionic fibers involved are components of the upper three thoracic nerves. Stimulation of the thoracic end of the cut cervical sympathetic trunk commonly results in bronchodilatation on one or both sides. The reaction is more marked, however, when the stimulation is applied to the upper thoracic rami."

We report the following case of blocking the sympathetic system from the level of the fourth interspace on the right side to and including the right stellate ganglion by alcoholic injections. The procedure is reported in detail, because we were able to induce, in man, a typical attack of asthmatic breathing, by electrical stimulation of this region. Moreover, we were able to stop the attack promptly by injecting alcohol into the same region.

Mrs. E. L., aged thirty-nine years, a housewife, married, with two children, applied for treatment (to C. A. S.) on February 20, 1926. She had been suffering from asthma since 1921.

Her family history was negative.

She has had rheumatism and headaches during her menstrual periods, and also has had bleeding piles. Her tonsils were removed in 1922.

Her first attack of asthma came on in 1921 after a cold; since then she has had attacks in the wintertime about once a month. The asthma grew progressively worse, until this past winter when it became constant and continuous. Her cough is almost continuous, nonproductive at times, while at others she brings up much yellow thick mucus. Most of her suffering occurs at night when she cannot lie down, but must sit up most of the time. Change of environment or vacation in the country had no effect on her condition.

Physical examination when she presented herself showed a well-developed and well-built woman, weight 169 lbs. Her skin was of good texture and color; the eyes, nose, and mouth showed no pathology; the teeth are all extracted and replaced by plates; the throat, neck, and chest, glands and heart showed no pathology but the blood pressure was 190/100. The percussion of the lungs was normal; auscultation showed sibilant and sonorous râles, as well as wheezing breath sounds, both on expiration and inspiration throughout both sides. Examination of abdomen and extremities showed no pathology.

The urine showed a faint trace of albumin, a moderate amount of indican, and a few hyaline casts. Blood Wassermann was negative. The sputum was negative for tubercle bacilli. X-ray pictures of the chest showed no pathology in the parenchyma of the lungs, and the heart and aorta appeared normal.

Protein tests were given with all the available pollens, animal emanations, dusts, silk, kapok, cotton seed, wool and orris, pyrethrum and tobaccos, all the cereals and wheats, eggs, meats, fishes, beverages, and all the vegetables, fruits and nuts—in all about 250 tests, with negative reactions.

Treatment was begun on February 20, 1926, with a polyvalent vaccine. This was continued to the end of 1926 with considerable improvement. She could walk around, do her housework, and the attacks which were now infrequent in occurrence, were less severe. The lungs, however, showed the physical signs of asthma continuously.

In February, 1927, asthmatic attacks returned with greater severity, and continued for the entire year in spite of all therapy. During 1928 the symptoms abated somewhat, and the attacks were less frequent, also more moderate. In 1929 she had attacks from January until July; from then to the end of the year she felt fairly comfortable. The asthma returned about January 1, 1930, and was very severe and constant, especially at night. This continued until January 23, 1930, when she entered the hospital. At that time the blood pressure had risen to 213/140.

Procedure.—In the x-ray department at 2:30 P.M. on the day of admission, one of us (E. L. S.) inserted a specially designed needle-electrode[12] into the fourth intercostal space on the right side. The paravertebral guard and guide for neurone blocking was used.[13] This is a modification of the spinal puncture guard.[14] Another needle-electrode was inserted into the second intercostal space on the same side. Both needle-elec-

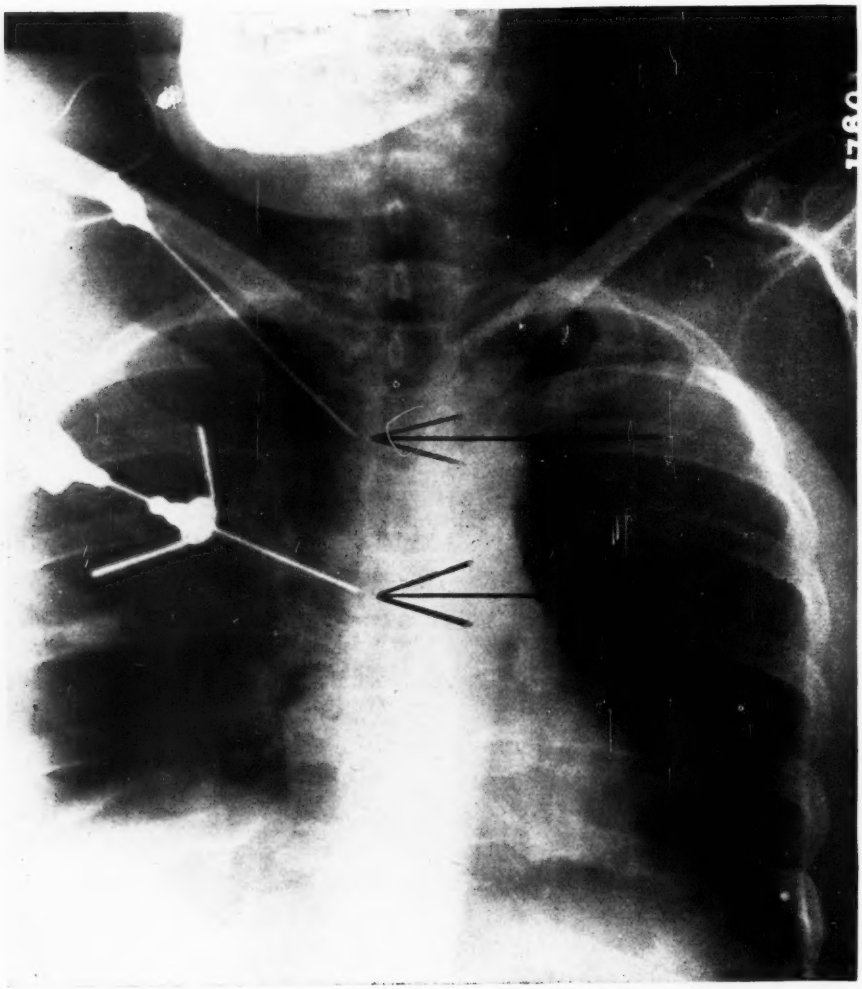

Fig. 1.—The needle-electrodes are shown in the regions of the second and fourth thoracic sympathetic enlargements (ganglia).

trodes were inserted to the region of the sympathetic trunk at these levels. Two wires were attached to these needle-electrodes, and a graph was taken by means of an Einthoven galvanometer, such as is used for making electrocardiographs. In this way it was hoped that some information might be obtained concerning the nature of any electrical impulses in this region. This is, as far as we know, the first attempt

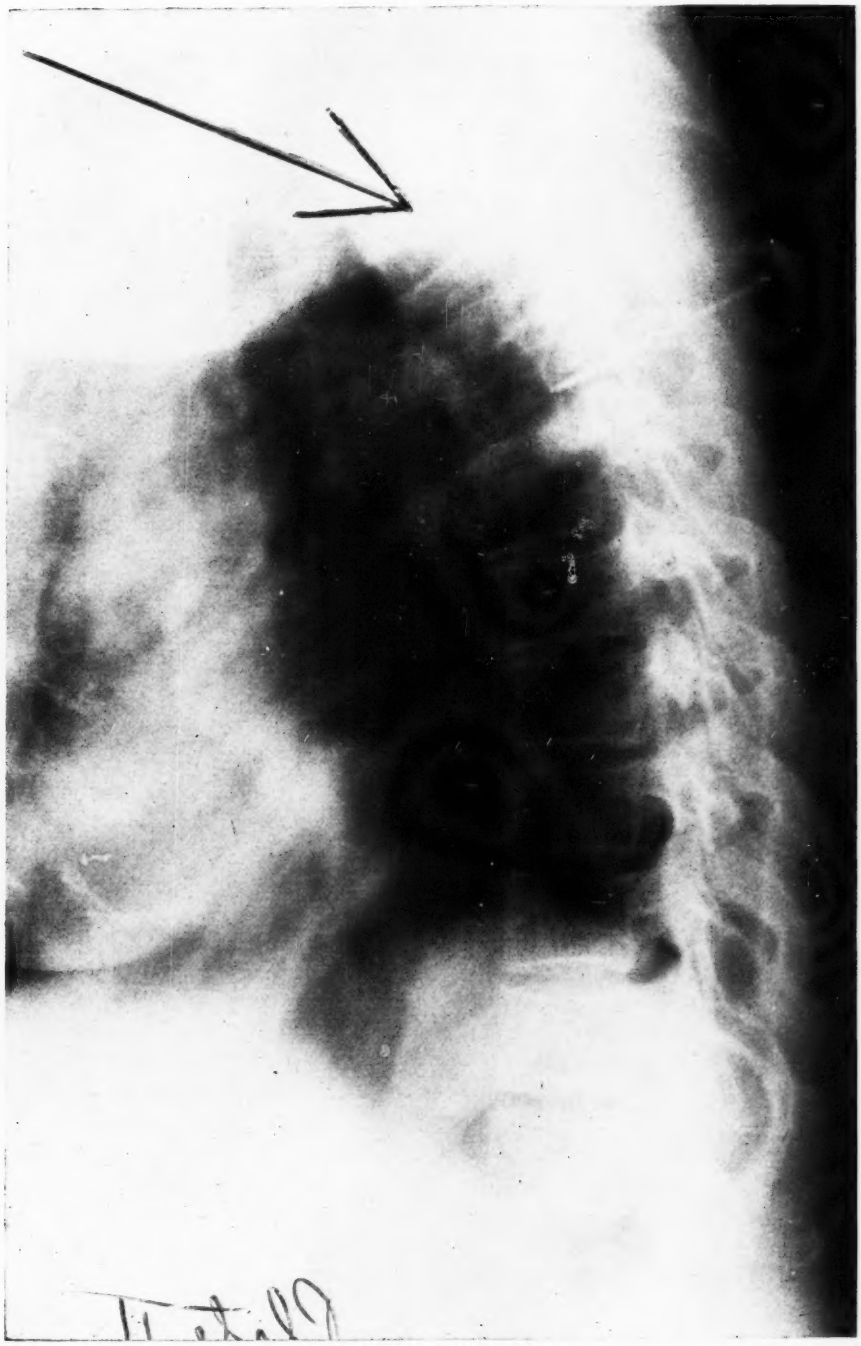

Fig. 2.—Side view showing the relation of the point of the needle-electrode to the intervertebral foramen.

to withdraw electrical impulses from the sympathetic system in man. The graphs obtained were not conclusive.

Stereoscopic x-ray pictures taken at this point showed that the points of the needle-electrodes were in or very close to the course of the sympathetic trunk in this region. Fig. 1 shows the needle-electrodes at the regions of the second and fourth thoracic enlargements (ganglia). Fig. 2 is a side view showing the relation of the point of the needle-electrode to the intervertebral foramen. Care was taken to make sure the points of the needle-electrodes were not in the pleural cavity or lung tissue, by attaching a water manometer to the needle-electrode before injecting any solution. We were also careful to aspirate after attaching the syringe, to make sure that the point was not in a blood vessel.

The needle-electrode (bipolar) in the fourth space was then connected with a weak faradic current, but there was no reaction as far as pain or shock, or muscular contraction could be determined by the patient or ourselves. A combined galvanic (4-6 m.a.) and faradic current was then applied, and again, there was no reaction.

Using the needle-electrode in the fourth space as one electrode, and the one in the second as the other, a slight faradic current was passed between them (between the second and fourth sympathetic ganglia). This caused the patient to experience an electric shock, and immediately she began to have typical asthmatic breathing, dyspnea, bronchial spasm, and wheezing. The right pupil became larger than the left.

A combined current of galvanic (4-6 m.a.) and slight faradic was then applied, and the patient complained of a slight "shaking" sensation along the right side of her spine. A combined current with 25 m.a. galvanic, caused an increased "shaking" sensation. We thought of the possibilities of leakage from the needle-electrodes through the spinal muscles, and this suggested further modification of the needle-electrode.

Through the needle-electrode in the fourth space, 7 c.c. of 95 per cent alcohol (containing 25 per cent NaI for x-ray purposes) were injected into and around the fourth sympathetic enlargement. With the first cubic centimeter of alcohol injected, the patient complained of severe pain lasting one to two minutes in the back and around the right side of the chest. Following this, the pain moderated and lasted about ten minutes. The injection of the remaining 6 c.c. during this time caused no aggravation of the pain. She did not cough and did not complain of any precordial pain. The asthmatic breathing induced by the electric current became less noticeable.

About twelve minutes after the start of the first injection, 7 c.c. of the same solution were injected through the needle-electrode into the region of the second sympathetic ganglion. This injection was less painful than the first. The patient complained of a moderate degree

of pain around the right side of the chest. She had no pain in her face. The asthma by this time was hardly noticeable. She also complained that the flesh around the posterior portion of the upper part of her right chest wall felt "like dead." An area of anesthesia was

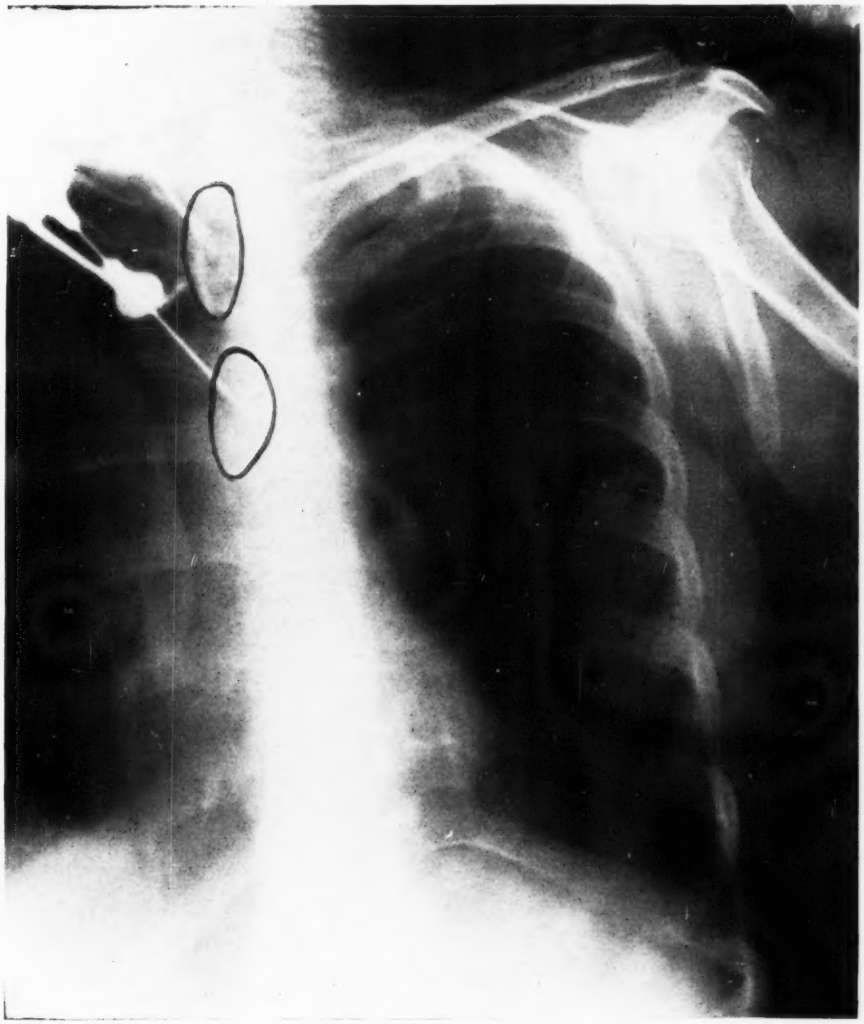

Fig. 3.—The needles and injected solution in situ.

found over this region. A flat plate to show the needles and the injected solutions in situ was then taken (Fig. 3).

These needle-electrodes were then removed. The patient was allowed to rest about ten minutes; and after the plates which were developed immediately were examined, the procedure was continued. A needle-electrode was inserted into the third intercostal space, to reach the region of the third sympathetic ganglion. Another needle-electrode was

introduced into the first intercostal space on the same side to reach the stellate ganglion and its environs.

The two electrodes were then attached to the Einthoven galvanometer, and again a graph was taken to record any electrical phenomena occurring between the stellate and the third sympathetic ganglion. It was hoped that as the region of the second ganglion was now blocked by the alcohol injection, this second graph might show some differences which might be attributable to the blocking effect. In this manner, we hoped to show by comparison of the two graphs, exactly what the nature of these sympathetic electrical impulses might be. As noted before, our interpretation and conclusions from this procedure were inconclusive.

An x-ray plate taken at this time showed the needle-electrodes in the desired positions. Seven c.c. of alcohol and NaI were then injected through the needle-electrode into the region of the third sympathetic ganglion. The patient again complained of pain around the chest, but this was definitely very much less than that which followed the very first injection. For only a moment she complained of pain in her chin. She also began to complain of feeling weak. Another 7 c.c. was then injected into and around the stellate ganglion on the right side. She complained of only a little pain, but her weakness increased.

A plate was then taken to show the needle-electrodes in the first and third spaces, and the injected solutions in the regions of the stellate, second, third, and fourth thoracic sympathetic ganglia. The needle-electrodes were then removed from the first and third spaces, and another plate was taken to show all the injected solutions in situ (Fig. 4).

The reaction of this procedure made the patient very weak. The blood pressure dropped from 213/140 to 110/70. The skin at all times was warm, but the pallor of the lips and the slight cyanosis around the nose and eyes, showed a shocked condition, or rather a marked state of depression. This, in our opinion, was due to the length of time consumed in the procedure, to the fact that she had to lie on a hard x-ray table during that time, and to the several small electric shocks that she had received. To a large extent, however, we believe that this depression was caused by the reaction of the sympathetic nervous system to the alcohol injected. Moreover, having had a high blood pressure as her normal, a rather sudden drop of the pressure to 110 systolic would also cause her to complain of weakness.

The patient was given 7 gr. caffeine hypodermically, warm blankets were applied, and she was removed to her room. The foot of the bed was raised, and she was given hot coffee and whiskey. She also received a hypodermic injection of 10 minims adrenalin. Her condition soon improved, and she was able to turn around in bed without assistance. Auscultation at this time revealed only very distant musical râles at the end of expiration on both sides of the chest. There was no dif-

ference in the chest signs between the right and left sides. At no time, even during the induced asthmatic attack, did the patient cough.

At 10:05 P.M. the same evening, the patient was found to have developed a definite Horner's syndrome. The right pupil was smaller than the left, and the right upper eyelid drooped a little. The con-

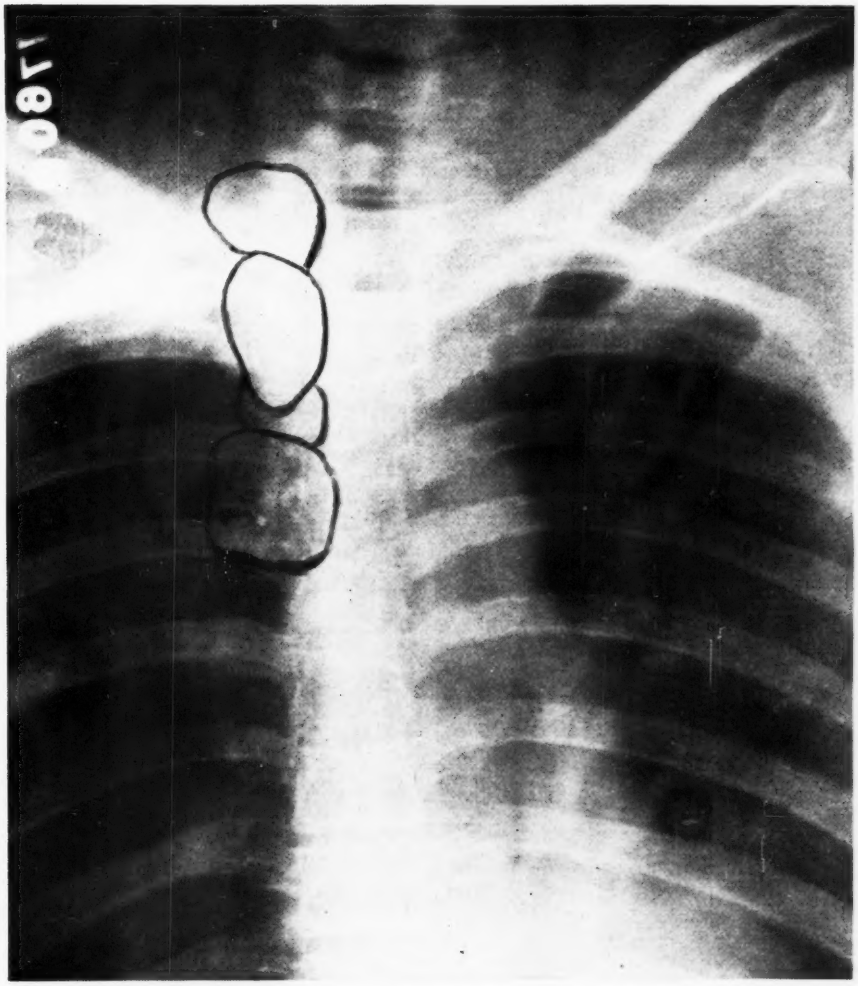

Fig. 4.—The injected solution in situ after withdrawal of the needles.

junctival vessels of the right eye were injected. She had neither pain in the chin nor itching.

Upon examining the chest, we found spasmodic expiration, with many rhonchi and râles on the left side. The right side was unquestionably *clear,* and there were no râles. Both sides were resonant. In other words, she had a *unilateral left-sided asthma.* The blood pressure was 182/110 on the right arm, 174/102 on the left arm. There were no

appreciable differences in the surface temperature of the upper extremities, although this was not accurately determined.

When seen again at 9 A.M. the next morning, the day after the injections, the Horner's syndrome was still present. She had had no attacks during the night, whereas she had had frequent attacks both day and night during the previous two weeks. She said, "It was the first night that I had no wheezing in four years." Her temperature was 101.3°, P. 106, R. 26. She was comfortable except when she moved around in bed. This motion produced pain in the back of her neck. She said her breast "felt full," and she complained of pain under the sternum on coughing.

Upon examining the chest, the breath sounds were found to be quiet on both sides, except for an area in the left axilla, and another area under the left clavicle where audible musical râles were heard. Both sides were resonant. She raised the right shoulder slightly more than normal on taking a deep breath. Her general condition was much improved.

During the day she was comfortable until about 5 P.M. when she had a slight attack of asthma. Between 5 and 10 P.M. there were short intervals during which time she had asthma. She stated she "felt more asthma" in the anterior and upper part of the right chest. At 10 P.M. the lungs were quite clear, except for some bronchospasm and râles heard in this area. The asthma which she complained of from 5 to 10 P.M. was very much milder than the attacks which she suffered during the two weeks previously. The pain and stiffness in the back of the neck were very much better, and she only complained of pain at the site of injections upon taking a deep breath. That night she slept at short intervals.

At 5 A.M. the following morning, the second day after the injections, the patient coughed up a plug of mucus about the size of her thumb, after which she breathed considerably easier. She had coughed up smaller plugs, ½ to ⅝ in. long, during previous heavy asthmatic attacks, but never anything so large.

When seen at 12:30 that noon, her condition was very good. The Horner's syndrome persisted. She still had pain on moving the right shoulder. Both sides of the chest were resonant and clear. The breath sounds were quiet and accompanied by a distant expiratory wheeze. There were no moist râles or rhonchi except at the upper part of the left chest, anteriorly, where a few rhonchi were heard.

When seen on the morning of the third day after the injections, the patient complained of having had a miserable night, with constant "bad asthmatic breathing." At about 9 A.M. she received 10 m. of adrenalin, and within five minutes she was relieved. At 10:30 the breath sounds on both sides showed prolonged expiration. and there were faint râles

throughout both lungs during expiration. The temperature, pulse, and respiration were normal.

The patient was allowed to go home on January 26. She had asthma for several subsequent nights. The course thereafter was as follows:

February 1, patient complained of much pain on the right side of the chest, reflected to the ensiform cartilage; the Horner's syndrome persisted.

February 3, patient complained of burning sensation in the right chest. The temperature in the right axilla was 99.3°, in the left 98.8°.

February 5, patient complained of pain in the right arm; the asthma was better, but she still was weak and unable to work.

February 8, no asthma; lungs were clear. On the right side the breath sounds were less audible than on the left.

February 11, no asthma; lungs were clear; however, patient complained of much pain in the right chest.

February 15, no asthma; lungs were clear; patient still complained of a little pain in the right chest and arm.

February 18 and 22, no asthma; lungs were clear.

March 4 and 5, patient had a slight attack of asthma.

March 11, 14, 18, and 21, moderate asthma.

SUMMARY

1. In a patient with bronchial asthma, stimulation of the sympathetic trunk between the level of the second and fourth intercostal spaces on the right side, by an electric current, induced an attack of asthmatic breathing.

2. Upon blocking this region with alcohol, the attack cleared up completely, and almost immediately.

3. Stimulation between the stellate ganglion and the level of the third intercostal space, after blocking the levels at the second and fourth spaces produced no attack of asthma.

4. Several hours after the blocking on the right side, the patient was found to have a *left unilateral asthma.*

5. Stimulation of the right sympathetic trunk from the level of the second to the fourth spaces, caused dilatation of the right pupil.

6. Blocking of the right sympathetic trunk by injections of alcohol, from the stellate ganglion to the region of the fourth thoracic ganglion, produced a Horner's syndrome of the right eye.

7. Blocking the right sympathetic from the stellate ganglion, to the region of the fourth thoracic ganglion, by means of alcohol injections, relieved a case of status asthmaticus for one month; i.e., the patient who had constant, repeated attacks of asthma, day and night, for about three weeks previous to the injections, had practically no asthmatic attacks of any severity, and the lungs were clear for almost an entire month *after* the injections.

8. A needle-electrode has been developed which can be used for electrical stimulating purposes at a depth from the surface of the body, and which, at the same time, can also be used as an ordinary needle for injection purposes.

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A SURVEY OF THE HERBACEOUS PLANTS IN NEW ORLEANS IN RELATION TO ALLERGY*†

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THE species of plants occurring in a given region are a product both of soil and of climatic conditions. In the New Orleans region the soil is alluvial and of a high water content and is thus capable of supporting forest vegetation. Since the climate is subtropical in nature one finds a mingling of tropical and temperate species and a considerable number of evergreen cultivated plants.

The original vegetation on the site of the present city was an extension of the deciduous forest common to most of eastern United States. On the other hand the species were quite different. Along the natural levees, willows, cottonwood, sycamore, water locust, Mississippi hackberry and red gum flourished, but the greater part of the city was occupied by cypress and tupelo. The soil in the city is mainly of Sharkey clay and muck, and these facts have a bearing on the species occurring in the city. Elsewhere in similar habitats but where the soil is lighter and higher the so-called cypress-tupelo-red gum forest gives way to longleaf, loblolly, and slash pines.

New Orleans is an industrial city with a population of 439,400 (1928 census). It is situated in a bend of the Mississippi River near Lake Pontchartrain and is approximately 100 miles from the Gulf of Mexico by way of the river. The climate, however, is essentially coastal because of the proximity of the city to the river, to Lakes Pontchartrain, Borgne, and Cataouatche, and since it is only an average distance of 50 miles from the Gulf of Mexico. The latitude is approximately 30° north and the longitude 90°-5′ west. The mean annual temperature is 69.1° F. with mean monthly temperatures of 54° F. and 82.4° F. for January and July respectively. The annual precipitation is 58 inches and very evenly distributed throughout the year. The average dates, over a period of ten years, for the last killing frost in the spring was February 14 and for the first killing frost in the fall was December 7. The above climate presents excellent growing conditions for ten months and enables many plants to continue their growth throughout the entire year.

The city of New Orleans presents a maximum of hay fever and asthma hazard because of the long and favorable growing season and the great amount of weedy vegetation in vacant lots and along drainage canals. One may find weed patches even in the business section,

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and they occur abundantly less than one mile from the heart of the business district. Careful estimates show that approximately 70 per cent of the land in greater New Orleans may be classed as weedy vegetation. This is much greater than that of Chicago. (Koessler and Durham, 1926.) Allergic diseases due to pollens occur throughout the year with a maximum in July, August, and September, but may, with certain individuals, be violent even in midwinter. The great prevalence of these diseases and the lack of knowledge concerning the causative agents furnished the necessary stimulus for surveys of the hay fever

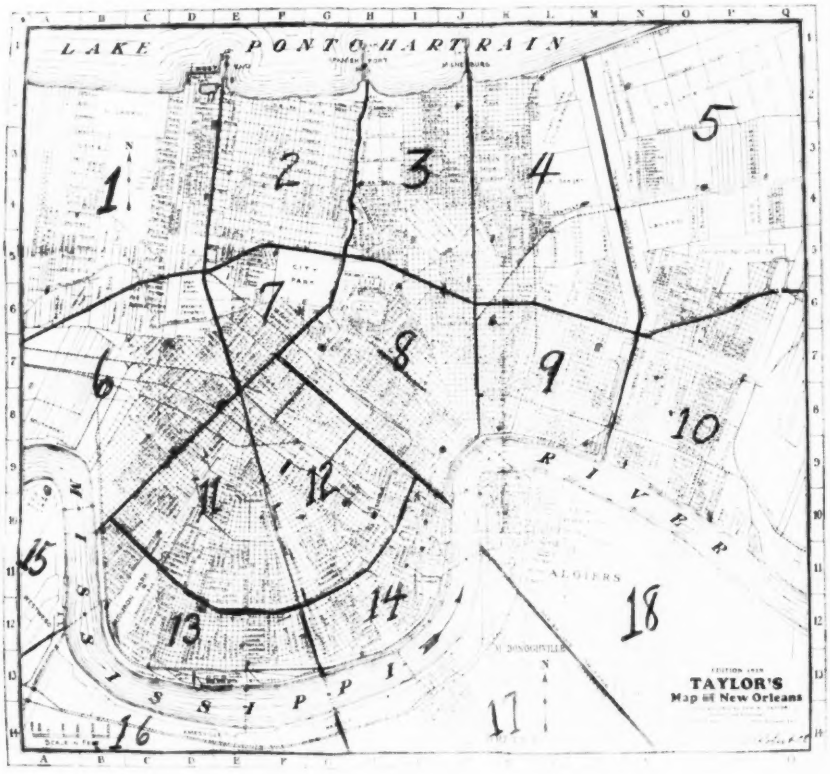

Fig. 1.

plants, for pollen counts, and for various researches on diagnosis and treatment. Only the first is being considered in this paper.

The survey here presented began on April 1, 1929, and ended on December 31, 1929. The city, including the suburbs of Algiers, Gretna, and Westwego, was divided into eighteen areas of large extent using conspicuous streets, canals, and the river as boundary lines (Fig. 1). Each area was visited at least once during the survey period. Since each area presented various growth conditions, an attempt was made to gather data from each habitat. Data were thus obtained in an average

of five stations for each area. The data were placed on sheets of paper 8½ x 11 inches and included number of area, date of survey, percentage of weedy vegetation, name of each species found, whether pollinating or in fruit, and its relative abundance, with the most abundant plant taken as 10.

The scientific names recorded in the table are taken from Small's *Flora of the Southeastern United States*—the synonym, in parentheses, from Britton and Brown's flora being given whenever the names were different in the two floras. The common names are all taken from Britton and Brown's flora except where none was given, in which case recourse was had to the common names extant in the New Orleans region. The figures in Table I refer to the relative abundance of the species studied and represent an average of the data obtained from eighteen different areas. Since no plant was found in every habitat and since no single plant was the most abundant in every area, the most abundant plant never had a relative abundance index of 10, the basis of comparison. Since only four species occurred in every area it is evident that the relative abundance index of a plant is no criterion as to its profusion in any given part of the city. It should also be clear that species of restricted range have a lower figure than those of greater frequence.

An analysis of the table shows that Bermuda grass has a relative abundance index of 7.0, the next highest being only 3.7. This is because of its profusion in lawns and parks throughout the city, to its long period of duration, and to the fact that it was found in every area and nearly every habitat studied. In addition it has a long period of anthesis, a rapid production of flowering stalks, often three days after being mowed, and profusion of pollen. Bermuda grass is thus, perhaps, the greatest hazard in pollen allergy. Nevertheless, the giant ragweed causes greater suffering because of its larger size and its tremendous production of small but very toxic pollen. The giant ragweed often forms dense stands in disturbed areas from 15 to 20 feet in height and under which few other plants can survive. Its related species, the lesser ragweed, is less widespread but occurs in weed patches and cemeteries throughout the city. This last statement is not in accord with that of Scheppegrell (1922).

The two bull grasses, together with Bermuda grass and giant ragweed, share the honor of being found in every area studied in the city. Since they pollinate for a long period and are of tall stature, it is presumed that they are of considerable importance in allergy. Of the two, the hairy bull grass is taller, more abundant, produces more flowers and has smaller pollen. In addition to the plants already discussed there are 22 species with a relative abundance index of more than 1. There is probably little doubt that all of these may be contributory factors in hay fever and asthma, but it does not follow that others with an

TABLE I

RELATIVE ABUNDANCE AND POLLINATING DATES OF HERBACEOUS PLANTS IN NEW ORLEANS THAT MAY CAUSE HAY FEVER

SCIENTIFIC NAME	COMMON NAME	POLLINATING DATES BEGIN HEIGHT END	ABUNDANCE
Acalypha virginica	Three-seeded mercury	April-May-Sept.	0.8
Amaranthus palmeri	Palmers amaranth	June-July-Oct.	0.4
Amaranthus powelli	Powells amaranth	June-July-Oct.	0.2
Amaranthus retroflexus	Redroot pigweed	June-July-Oct.	0.6
Amaranthus spinosus	Spiny amaranth	May-June-Nov.	1.0
Amaranthus viridis	Green amaranth	May-June-Nov.	1.2
Ambrosia artemisiifolia (Ambrosia elatior)	Lesser ragweed	July-Aug.-Nov.	2.2
Ambrosia trifida	Giant ragweed	July-Aug.-Dec.	3.4
Anastrophus compressus	Louisiana grass	May-June-Nov.	1.5
Anastrophus platycaulis	Longhorn grass	May-June-Nov.	1.3
Andropogon glomeratus	Bushy beard grass	Sept.-Sept.-Nov.	1.5
Andropogon virginicus	Virginia beard grass	Aug.-Aug.-Oct.	0.3
Bohemeria nivea	Ramie	June-July-Sept.	0.3
Brachiaria platyphylla	Maiden cane	May-June-Aug	0.1
Bromus unilioides	Southern chess	March-April-June	1.2
Capriola dactylon	Bermuda grass	April-May-Dec.	7.0
Cenchrus tribuloides	Sand bur	April-May-July	0.3
Chaetochloa glauca	Yellow foxtail	April-May-Oct.	2.0
Chaetochloa magna	Giant foxtail	July-Aug.-Sept.	0.3
Chenopodium album	Lamb's quarters	June-Aug.-Oct.	0.2
C. anthelminticum	Wormseed	April-June-Dec.	1.5
Eatonia pubescens (Sphenopholis obtusata)	Early bunch grass	March-April-May	0.8
Echinochloa colona	Jungle rice	April-May-Nov.	1.2
Echinochloa crus-galli	Barnyard grass	April-May-Nov.	0.5
Echinochloa walteri	Salt marsh cockspur	May-July-Sept.	0.1
Eleusine indica	Yard grass	April-May-Nov.	2.4
Elymus virginica	Terrell grass	April-May-June	0.5
Erianthus saccharoides	Plume grass	Sept.-Oct.-Nov.	0.3
Eupatorium capillifolium	Dog fennel	May-July-Sept.	2.3
Hordeum pusillum	Little barley	March-April-May	1.6
Iva ciliata	Marsh elder	Sept.-Sept.-Nov.	3.2
Iva frutescens	Shrubby marsh elder	Aug.-Aug.-Oct.	0.1
Leptilon canadense	Horseweed	April-May-Nov.	1.6
Leptochloa attenuata	Slender grass	June-July-Aug.	0.1
Lolium multiflorum	Winter grass	April-May-July	0.3
Panicum proliferum	Ditch grass	May-June-Aug.	1.3
Panicum rostratum	Panic grass	May-June-July	0.2
Paspalum boscianum	Bosc's Paspalum	July-Aug.-Sept.	0.1
Paspalum dilatatum	Tall bull grass	April-May-Nov.	3.5
Paspalum mucronatum	Water Paspalum	July-Aug.-Sept.	0.4
Paspalum distichum	Devil's grass	July-Aug.-Sept.	1.0
Paspalum vaseyanum	Hairy bull grass	April-May-Nov.	3.7
Phalaris canariensis	Canary grass	April-May-June	0.1
Phleum pratense	Timothy	April-May-June	0.1
Plantago lanceolata	Buckhorn	April-May-Nov.	0.1
Plantago major	Common plantain	March-May-Dec.	0.3
Plantago virginica	Virginia plantain	March-May-June	0.4
Poa annua	Annual blue grass	Jan.-March-May	2.0
Polygonum aviculare	Doorweed	April-June-Oct.	0.2
Ricinus communis	Castor bean	April-May-July	0.2
Rumex crispus	Sour dock	March-May-Nov.	0.4
Rumex pulcher	Fiddle dock	April-May-July	0.5
Rumex verticillatus	Swamp dock	April-May-Nov.	1.0
Sacciolepis gibba	Gibbous panic grass	June-July-Sept.	0.1
Sorghum halapense (Holcus halapensis)	Johnson grass	April-May-Nov.	2.5

TABLE I—CONT'D

SCIENTIFIC NAME	COMMON NAME	POLLINATING DATES BEGIN HEIGHT END	ABUNDANCE
Sporobolus indicus (S. angustus)	Smut grass	April-May-Oct.	2.8
Syntherisma fimbriatum	Crab grass	April-May-Nov.	2.5
Typha latifolia	Cat-tail	April-May-June	0.6
Xanthium speciosum	Cocklebur	July-Aug.-Oct.	2.3
Zea mays	Corn	April-May-July	0.5
Zizania aquatica	Indian rice	April-May-Aug.	0.1

NOTE.—The relative abundance index of each species is an average of the data obtained in eighteen different areas.

index less than 1 are of no importance. In fact it is definitely known that some of these species may be of considerable importance locally or during the height of their period of anthesis.

The relative percentage abundance of the more numerous species was calculated from the indices in Table I and are presented in Table II. An analysis of the data shows that a considerable number of species have a percentage abundance of more than 15. In fact our survey shows more than twice the number of such species than did that of Koessler and Durham (1926) in the Chicago area. In addition the data here presented indicate that New Orleans is predominantly a region of grasses, whereas the Chicago region is dominated by the ragweed group.

TABLE II

RELATIVE PERCENTAGE ABUNDANCE OF THE MORE COMMON HERBACEOUS PLANTS IN NEW ORLEANS THAT MAY CAUSE HAY FEVER

Bermuda grass	100	Horseweed	23
Hairy bull grass	53	Little barley	23
Tall bull grass	50	Wormseed	21
Giant ragweed	48	Bushy beard grass	21
Marsh elder	46	Louisiana grass	21
Smut grass	40	Longhorn grass	18
Johnson grass	36	Ditch grass	18
Crab grass	36	Green amaranth	17
Yard grass	34	Southern chess	17
Dog fennel	33	Jungle rice	17
Cocklebur	33	Spiny amaranth	15
Lesser ragweed	31	Devil's grass	15
Yellow foxtail	28	Swamp dock	15
Annual blue grass	28	All others—less than	15

BY GROUPS

Grasses	100
Ragweeds	29
Composites	10
Amaranths	5
Chenopods	4
Docks	2

The pollinating dates of a given species in New Orleans are very difficult to determine because of variation in soil moisture, in dates of first and last frosts, in time of cutting lawns and weed patches, and to the amount of disturbance of the soil. In addition, the data here pre-

sented have been prepared from detailed observations over one growing season only, although miscellaneous records for the past three years have been resorted to. It is recognized also that perhaps 40 per cent of the species may, during years of favorable conditions, bloom throughout the entire year. The data in Table I are, however, of considerable value, since they are the only authentic records for the region in question.

In any discussion of pollen allergy it has been customary to divide seasonal cases into definite groups. Duke (1925) divided the seasonal cases of Kansas City into the spring or tree season, the late spring or grass season, and the autumn or ragweed season. This has been the scheme followed by most investigators on this subject. Scheppegrell (1922) gave May 5 to July 25 for the combined spring and summer form and August 2 to October 16 as the dates for the autumn form. The seasons for the New Orleans region are, however, less distinct and of greater duration than those given by Scheppegrell.

On the basis of their period of anthesis the species in New Orleans may be grouped into:

1. Winter bloomers (January 1 to April 1). This season includes most of the trees and the annual blue grass.

2. Spring bloomers (April 1 to July 1). This season includes Terrell grass, winter grass, early bunch grass, sandbur grass, little barley, timothy, and cat-tail. It is preeminently a grass season.

3. Autumn bloomers (August 1 to December 1). This season actually includes only five species, namely: bushy beard grass, Virginia beard grass, plume grass, marsh elder, and the shrubby marsh elder. Since many others begin to bloom only in late July, it is perhaps safe to include here the two ragweeds, cocklebur, giant foxtail, water paspalum, and devil's grass. Although a greater number of grass species bloom during this season the ragweeds and marsh elder are the most prolific pollinators.

4. Ever-bloomers (April 1 to December 1 or a major part thereof). This group includes most of the important grasses, the amaranths, chenopods, docks, and plantains. It is the most important group of allergic plants in the city and causes hay fever and asthma at any time, especially after a rainy period or when second crops follow disturbed conditions or cutting.

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Department of Reviews and Abstracts

Selected Abstracts

New Method of Administering Pollen Extract for Purpose of Preventing Reactions. Duke, W. W.: J. A. M. A. **94**: 767, 1930.

The method described is based upon the theory that reactions are due, not to a long-continued effect of any given amount of pollen, but to a too rapid rate of dissemination of pollen from the site of inoculation to the body tissues generally. A control of this rate of dissemination may be obtained by following four important steps:

1. The placing of a rubber turniquet around the arm above the site of injection of pollen and just prior to it. This tourniquet should be removed and replaced for at least five minutes after the injection, at intervals of about thirty seconds. If, on release of the tourniquet at any time, the patient begins to experience those symptoms associated with a reaction, the tourniquet should be immediately reapplied.

2. The admixing of epinephrine and ephedrine with the pollen solution in such dosage as to slow down its rate of dissemination from the site of injection. A solution of two parts of ephedrine (3 per cent) with one part of epinephrine (1:1,000 solution) is advised as a suitable mixture to add to pollen extract. If a greater quantity of epinephrine is added, the patient may experience pounding of the heart and cardiac arrhythmia.

3. The introduction of 0.01 c.c. of the pollen mixture subcuticularly (just beneath the skin) preliminary to the injection of the entire mixture. If a tiny, blanched area appears, the needle is not in a vein, and the rest of the mixture may safely be administered. This method has the further advantage of leaving fewer scars.

4. The reduction of all doses to a given volume by the admixture of physiologic solution of sodium chloride.

The Control of Immediate Shock Following Hypodermic Medication. (Preliminary Report.) Insley, S. W.: J. A. M. A. **94**: 765, 1930.

The use of a blood pressure cuff is advocated as a means of controlling constitutional reactions in immunizing therapy. The cuff is adjusted just above the injection area. Two case reports are given at length, in which this agent was used to advantage.

Experience showed that pressure need not necessarily be sufficient to cut off the arterial flow but should be sufficient to cut off not only

venous return but also lymphatic seepage. In such manner, the rate of absorption for subcutaneous injections of medicaments can be controlled. By use of the pressure cuff less reliance need be placed upon ephedrine, epinephrine and similar drugs for the balancing of shock.

The General Health and Mental Activity of Allergic Children. Balyeat, R. M.: Am. J. Dis. Child. **37:** 1193, 1929.

A study of the general health of three hundred and twenty-three allergic children, with a hypersensitive condition which was demonstrated by positive intradermal tests, is presented with a study of the mental activity of eighty allergic and eighty nonallergic children. The Otis self-administering test of mental activity was the one used for the determination of the intelligence quotient. The classification used was Terman's.

The conclusions are that a large percentage of allergic children are normal or above normal in general health and have a superresistance to pathogenic organisms. The mental activity of allergic children apparently is far above the average normal.

Ragweed Dermatitis: With Sensitization and Desensitization Phenomena. Sulzberger, M. B., and Wise, F.: J. A. M. A. **94:** 93, 1930.

A report is given in detail of a case of dermatitis due to ragweed sensitization. The patient complained of a skin disease that had been recurring in the late summer and fall for the past ten years. There was no family history of allergic disease. The patient was tested by the scratch method to a large variety of pollens including giant and short ragweed. The results of these tests were negative. Tests were then made with the same substances by the contact method, i.e., the substances were applied to the uninjured skin and kept in contact with it for twenty-four hours.

Twenty-four hours after the contact tests, there was a marked reaction at the site that had been in contact with short ragweed allergen. Desensitization was attempted, not by the usual methods, but by the intradermal route. Thus, the site of injection was changed from deeper tissue to the most superficial part of the skin that can be reached by injection treatment. Intradermal injections were given approximately three times a week from August 9 to September 4. The initial dose was 0.1 c.c. of Lederle's Ragweed Pollen Allergen, dose 1, in one area, and this was gradually increased, the final dose being 0.1 c.c. each of dose 10 in three areas, totaling 0.3 c.c. After the completion of the course, the patient was again tested by contact with ragweed allergen with negative results. The patient's symptoms were much improved.

The authors stress the importance in certain dermatitis cases of the use of the contact test and the employment of the intradermal method of desensitization.

Flax Hypersensitiveness. Black, W. C.: J. A. M. A. **94**: 1064, 1930.

Two cases are reported in which severe reactions of an allergic character followed the consumption of a breakfast food called Roman Meal. The composition of this cereal was stated on the container to be wheat, rye and flax. Cutaneous tests by the scratch method were performed with the Roman Meal and with the proteins of wheat, rye, flaxseed and flax. Strong positive reactions were obtained with Roman Meal and flaxseed.

It was assumed that flaxseed or flax meal was incorporated in the cereal, the content being somewhat loosely designated as flax.

Both patients gave a history of previous contact with flaxseed in the form of poultices. Both patients gave a history of hay fever and asthma.

Allergic Insulin Reactions. Williams, J. R.: J. A. M. A. **94**: 1112, 1930.

Allergic reactions from the administration of insulin which is a protein-bearing compound, have often been encountered. They are usually mild in nature, limited to a local skin reaction, and may be easily corrected by the oral use of calcium lactate. Occasionally, however, severe reactions involving the gastrointestinal tract and other portions of the body occur.

A case is reported in detail in which, apparently, hypersensitiveness to the protein in the type of insulin used, almost caused the death of the patient. The patient, a child of twelve years, had been unable to tolerate food for eight days and was suffering severe abdominal distress. The patient was a diabetic under insulin treatment. The insulin used was derived from the pancreas of the pig. Upon the substitution of an insulin derived from beef pancreas, a startling improvement immediately took place in the patient. Within forty-eight hours, he was eating solid food. The inference of the author is that the patient was suffering from an allergic attack involving the pyloric end of the stomach and due to pig protein.

It is suggested that manufacturers of insulin mark on the package the animal source of the product.

Sensitization to Saprophytic Fungi in a Case of Eczema. Hopkins, J. G., Kesten, B. M., and Benham, R. W.: Proc. Soc. Exper, Biol. and Med. **27**: 342, 1930.

In the case reported, the patient had a chronic eczema involving the hands and feet, and to a lesser degree, the forearms and legs. The

patient also suffered from asthma. The asthma, in a previous report, was ascribed to a saprophytic fungus (altenaria). Positive skin reactions were obtained with extracts of the fungus, and passive transfer of sensitivity was demonstrated. Inhalation of a spray of an extract of the fungus also produced characteristic paroxysms of asthma.

It has been reported that patients with eczema may be sensitized to saprophytes which grow in their lesions. In the present instance immediate intradermal skin reactions could be obtained to extracts of the fungus which caused the asthma, to aspergillus which was obtained from the skin and to extracts of other fungi obtained from house dust. Surface tests with fungus extracts also called forth a mild skin irritation. On several occasions following the production of asthma by altenaria spray, a patch of eczema became acutely inflamed.

The admitted difficulty is that the known sensibility of eczematous skin to nonspecific irritation throws uncertainty upon the significance of the reactions.

Schistosomiasis of the Lungs Simulating Bronchial Asthma. Suarez R. M.: Bol. Asoc. méd. de Puerto-Rico **21**: 40, 1930.

A case report is given in detail of a patient suffering from cough with some nocturnal exacerbation, some dyspnea and a tired feeling, all of five months' duration. There was no family history of allergy. The patient's cough, dyspnea and mucous sounds in the chest were worse at night. Blood examination showed an eosinophilia of 74 per cent. Skin tests, however, were negative for the common foods and epidermals. Examination of feces showed a few ova of the *Schistosomun mansoni.*

A review of the literature on schistosomiasis reveals the fact that lung pathology has been noted in connection with the disease, and there is frequent mention of bronchitis associated with or preceding intestinal or dysenteriform symptoms of schistosomiasis.

The author expresses the opinion that the case in question is an example of schistosomiasis of the lungs simulating bronchial asthma.

Allergy and Acidosis. Choremis, K.: Klin. Wchnschr. **8**: 1817, 1929.

Investigation was undertaken to determine a possible relationship between allergy and acidosis. Three children were selected who had been shown repeatedly to be positive to tuberculin. In order to influence the metabolism of these children, hydrochloric acid, in addition to their usual diet, was given to them over a period of three and one-half months. Daily increasing doses from four to thirty drops were given. The acidosis was estimated through the P_H determination of the urine and through the Van Slyke determination of the alkaline

reserve. Results showed that during the period of acid metabolism of the organism there was a distinct lessening of the allergic symptoms as manifested both by a decrease in size and duration of the tuberculin reaction and by a decrease in infiltration.

Tables are given. Further investigation of the question is in progress.

Clinical Observations on Phenylaminoethanol Sulphate. Piness, G., Miller, H., and Alles, G. A.: J. A. M. A. **94**: 790, 1930.

Studies have been carried out on phenylaminoethanol sulphate in the effort to produce a substance that would cost less than ephedrine and that would have a prolonged effect and at the same time avoid the unusual toxic effect which goes with ephedrine.

Phenylaminoethanol sulphate, applied locally in the nose causes a marked shrinking and paling of the mucous membrane without irritation. A 2 per cent solution was used as a routine on a few hundred patients to relieve the coryza and nasal obstruction of hay fever. The relief was rapid but the duration variable. The compound was most effective when administered intravenously. It had little effect when administered subcutaneously and none when administered orally. This fact constitutes the chief drawback of phenylaminoethanol sulphate. The absence of physiologic activity upon oral administration is interesting from a chemical standpoint. The substance differs from ephedrine in chemical structure only in that it contains two less methyl groups. It was considered possible that the presence of one or both of these methyl groups in the molecule might be causally related to the effectiveness of ephedrine when administered orally. Upon investigation with other compounds, this proved to be the case.

Hyposulphate of Magnesium and Anaphylactic Shock. Lumiére, A., and Malespine, Mme.: Compt. rend. Soc. de biol. **100**: 351, 1929.

Experiments were carried out to determine the protective value of hyposulphate of magnesium against anaphylactic shock.

Guinea pigs were sensitized by the subcutaneous injection of 1 c.c. of horse serum diluted 1-50. At the end of forty-five days, sensitivity was tested by the intracardiac injection of 0.5 c.c. of the same horse serum mixed with 0.5 c.c. of physiologic serum. The test animal responded with a severe anaphylactic shock which proved to be just short of lethal.

Another pig from the same lot was given by the intracardiac route the same dose of horse serum (0.5 c.c.) but mixed with 0.5 c.c. of solution of hyposulphate of magnesium 1-10.

This animal gave only slight symptoms of distress which disappeared completely in four or five minutes.

When, in other animals, the protective dose of hyposulphate of magnesium was diminished, the symptoms of shock became more severe.

Comparison was then made between the protective power of hyposulphate of magnesium and the corresponding sodium salt. It was shown that the magnesium compound was approximately twice as active as the sodium compound.

In conclusion, the authors state:

1. Hyposulphate of magnesium mixed with the shocking dose protects the sensitized animal against anaphylactic shock.

2. With weak doses of hyposulphate of magnesium, the protection is not instantaneous and is less effective, but still exists.

3. Hyposulphate of magnesium is much more effective than hyposulphate of sodium as a protective agent against shock.

A Proof of Increased Capillary Permeability in Anaphylactic Purpura and Other Conditions. Basch, F.: Klin. Wehnschr. **8**: 1817, 1929.

In Henoch's or anaphylactic purpura, the thrombocytes in the blood are normal. The purpura is due to damage of the capillary wall with increased permeability. A similar manifestation occurs in nephritis and nephrosis. The edema in these cases occurs when the capillary pressure rises. To show the rôle of the capillaries in these conditions, children suffering from them were examined. It was found that children who remained standing for a period of two hours, diuresed less because the increased hydrostatic pressure in the capillaries in this position in addition to the injured capillary walls permitted a transudation into the tissues themselves. Water, therefore, entered the tissues rather than coming out through the urinary passages. On the other hand, when children were lying down and the hydrostatic pressure was thus lessened, much greater diuresis occurred. A table is given showing this marked discrepancy. The occurrence of nephritis with Henoch's purpura may thus be explained.

Studies in Hypersensitiveness. XXXVI. A Comparative Study of Antibodies Occurring in Anaphylaxis, Serum Disease and the Naturally Sensitive Man. Cooke, R. A., and Spain, W. C.: J. Immunol. **17**: 295, 1929.

A comparative study was made of the reacting bodies in the serum of naturally sensitive man (asthma), of the artificially sensitized man (serum sickness) and of the animal (anaphylaxis). Experiments were carried out to determine the ability of each serum to sensitize normal human skin and the smooth muscle fiber of the uterus of the guinea pig, and to determine the presence or absence of precipitin.

The first series of experiments dealt with the serum of naturally sensitive man. Attempts were made to demonstrate:

A. Passive transfer of sensitiveness to normal human skin.

B. Passive transfer of sensitiveness to the experimental animal.

C. Precipitin content.

A. Sera from twelve hypersensitive individuals were employed. Transfer was made to the skin both of normal individuals and of individuals who were allergic but not sensitive to the specific protein content of the test serum. Results showed that in both types of individuals, upon reinjection at the original site of the offending protein, marked reactions occurred. Control tests were made. Results showed that the serum from the naturally sensitive patients possessed to a marked degree the ability passively to sensitize the skin of a normal individual.

B. In the twelve sera employed not one instance could be shown by the Dale method of the passive transfer of sensitiveness to the experimental animal. The ability of the muscle to become passively sensitized was verified by the use of egg white as a control.

C. In none of the twelve sera employed, could precipitin be demonstrated.

The second series of experiments dealt with the serum of artificially sensitized man. In similar manner, attempts were made to demonstrate:

A. Passive transfer of sensitiveness to normal human skin.

B. Passive transfer of sensitiveness to the experimental animal.

C. Precipitin Content.

A. Four sera were used, obtained from cases of serum disease. In these patients a sensitivity to horse serum had been induced by original therapeutic injections of antipneumococcus serum or antidiphtheria or antitetanus serum. Passive transfer was made with these sera with the same technic previously employed. Individuals were chosen of whom some were normal and some were asthmatic patients, not, however, sensitive to horse serum or horse dander. Passive transfer was easily demonstrated.

B. Passive transfer of sensitiveness to the experimental animal was proved by the positive Dale reaction in one case.

C. Precipitin was found to be present in two of the sera and absent in two.

The third series of experiments dealt with the serum of the artificially sensitized animal. The same régime was used as in the other two series of experiments.

Six anti-egg-white rabbit sera were used.

A. Passive transfer of sensitiveness to the normal human skin could be demonstrated in but three of the sera.

B. Passive transfer of sensitiveness to the experimental animal by the Dale method was demonstrated by all six sera.

C. Precipitins were demonstrated in all sera.

In conclusion it is stated that the serum of naturally sensitive man shows a regular presence of skin sensitizing bodies and the regular absence of muscle sensitizing bodies.

The serum of artificially sensitized man shows the presence of skin sensitizing bodies in some samples where the presence of muscle sensitizing bodies is not demonstrable.

The serum of sensitized animals shows the presence of muscle sensitizing bodies in some samples where the presence of skin sensitizing bodies is not demonstrable. It is to be concluded that skin sensitizing and smooth muscle sensitizing antibodies are separate and distinct.

To date, no fundamental differences between the skin sensitizing antibodies present in the three types of sera, have been demonstrated.

Hereditary Transmission of Anaphylaxis. Nattan-Larvier, L., and Richard, L.: Compt. rend. Soc. de biol. **101:** 636, 1929.

The question is raised whether an active sensitization may be obtained in the newborn by the passage through the placenta of heterologous serum injected into the pregnant female. Experiments are given to show that such a sensitization may occur. Evidence points, however, to the fact that it is rare. There are many negative results. It is suggested that the amount of heterologous serum that passes through the placenta and penetrates into the organism of the fetus is too weak, in general, for sensitization.

Exceptional instances are recorded where the dose has been sufficient for sensitization. A female guinea pig received 3 c.c. of antidiphtheria serum subcutaneously. The litter was born less than twenty-four hours later. One of the litter, twenty-four days after birth, at a weight of 180 gm. showed characteristic symptoms of anaphylactic shock after an intracardiac injection of 1 c.c. of normal horse serum. Other instances are cited. A sensitivity of this origin is not necessarily acquired by each animal in the litter.

The anaphylaxis which is determined through sensitization through the placenta presents the usual characteristics of active anaphylaxis. If the injection of serum into the pregnant guinea pig has been made a short time before the birth of the litter, the young are not sensitive at the moment of birth and do not become so until fifteen or more days have elapsed. The sensitivity, like all active sensitization, lasts for three or four months.

Opposed to this, the newborn who have acquired a passive sensitization during intrauterine life can be subject to anaphylactic shock from the day of their birth, but lose their sensitivity, ordinarily, in less than three months.

It is stated that an anaphylaxis determined by the passage of heterologous serum through the placenta is not to be considered an hereditary anaphylaxis.

Attempted Transfer to the Rabbit of Pollen Hypersensitivity in Man. Vallery-Radot, P., Giroud, P., and Thigo, A.: Compt. rend. Soc. de biol. 101: 893, 1929.

In the experiments the serum from human beings hypersensitive to Dactylis glomerata and giving a strong skin reaction to an extract of this pollen was used.

Four male rabbits were injected subcutaneously and two male rabbits intravenously with serum taken twenty-four hours previously from subjects sensitized to the pollen extract of Dactylis glomerata.

The injection doses varied between 25 and 40 c.c. The doses were fractionated and given at several days interval. The shocking dose was given intravenously with the extract of Dactylis glomerata twenty-four hours after the last serum injection. The amount given was from 1 to 2 c.c. The arterial pressure was taken immediately after the injection, and for one-half hour thereafter. The pressure remained unchanged, and there was no evidence of shock. Similar attempts upon guinea pigs had also produced negative results.

An attempt to demonstrate passive transfer of hypersensitiveness to rabbits by the Prausnitz-Küster method gave negative results. It is well to know that this method gives positive results in man.

The authors conclude that the passive transfer reaction is not identical in man and in animals.

The Action of Ephedrine, Pseudoephedrine and Epinephrine on the Bronchioles. Swanson, E. E.: J. Pharmacol. & Exper. Therap. **36**: 541, 1929.

A review is given of the literature on the pharmacologic action of ephedrine, with a discussion of the results obtained by various workers. Chen and his coworkers and Read and his associates agree that the outstanding effects of ephedrine are due to its stimulation of the sympathetic nervous system. But some doubt has been expressed by other workers as to whether ephedrine is a true sympathetic acting drug. The present paper, in an attempt to clarify the situation, is a report on the bronchodilator action of epinephrine, ephedrine, and pseudoephedrine on pithed dogs.

In the first experiments, the findings of Brodie and Dixon, Jackson, and others, to the effect that bronchial movements are independent of circulatory changes, were verified. A plethysmograph was inserted into the chest of a dog. The dog was then pithed. The plethysmograph contained a "T" tube. One end was connected with a pump; the other end, which controlled the intake or equalized the vacuum produced by the pump during aspiration, was controlled by a screw clamp. The tambour was attached by a rubber tube to the tracheal cannula. When inspiration was desired, the tambour was attached by

a rubber tube to the plethysmograph and the pump line to the tracheal cannula. By this method decided increases and decreases in the blood pressure were recorded with no change in the bronchioles. Stimulation of the nerves by pilocarpine produced a distinct bronchoconstriction, and a bronchodilatation was caused by epinephrine.

Further experiments with the plethysmographic method showed that partial or complete paralysis of the sympathetic nerve endings by ergotamine and ergotoxine did not prevent or inhibit the bronchoconstrictor action of arcoline, pilocarpine, physostigmine, morphine, diethylmorphine, and histamine. The bronchoconstrictor action of these drugs after injections of ergotamine and ergotoxine was abolished temporarily by epinephrine and permanently by ephedrine and pseudoephedrine. Ephedrine is more active as a bronchodilator than pseudoephedrine. The bronchodilator action of epinephrine was shown to be more powerful than that of either ephedrine or pseudoephedrine, which, while slower were more prolonged in their action.

After partial or complete paralysis of the motor and sensory nerve endings by cocaine, the bronchoconstrictor action of pilocarpine, arcoline, and physostigmine was abolished by ephedrine, pseudoephedrine, and epinephrine. The epinephrine dilator action was increased by cocaine, but ephedrine and pseudoephedrine were partially inhibited by cocaine. The bronchodilatation of ephedrine was less inhibited by cocaine than that of pseudoephedrine.

Epinephrine, then, is shown to be a neurotropic acting drug and ephedrine and pseudoephedrine to be both neurotropic and musculotropic acting drugs.

In conclusion, the authors state that epinephrine, ephedrine, and pseudoephedrine have different types of action on the sympathetic nervous system, but these differences are insufficient to exclude ephedrine and pseudoephedrine as sympathomimetic acting drugs. The article carries detailed protocols and figures.